THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

COMPOUNDS WITH
CONDENSED THIOPHENE RINGS

This is the seventh volume published in the series
THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

A SERIES OF MONOGRAPHS

ARNOLD WEISSBERGER, *Consulting Editor*

COMPOUNDS WITH
CONDENSED
THIOPHENE RINGS

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The Chemistry of Heterocyclic Compounds

The chemistry of heterocyclic compounds is one of the most complex branches of organic chemistry. It is equally interesting for its theoretical implications, for the diversity of its synthetic procedures, and for the physiological and industrial significance of heterocyclic compounds.

A field of such importance and intrinsic difficulty should be made as readily accessible as possible, and the lack of a modern detailed and comprehensive presentation of heterocyclic chemistry is therefore keenly felt. It is the intention of the present series to fill this gap by expert presentations of the various branches of heterocyclic chemistry. The subdivisions have been designed to cover the field in its entirety by monographs which reflect the importance and the interrelations of the various compounds, and accommodate the specific interests of the authors.

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ARNOLD WEISSBERGER

Preface

The chemistry of compounds containing the condensed thiophene nucleus was originally scheduled to be included in the volume, *Thiophene and Its Derivatives*. However, since the material collected on the several hundred condensed systems containing a thiophene nucleus was so voluminous and diverse, it seemed advisable to treat this subject in a separate volume.

The two volumes have been designed to cover critically all phases of the chemistry of the thiophene systems. Thus, whenever it has been possible, physical constants, reaction conditions, yields, and other pertinent data have been included. An exception was made in the case of the thioindigo dyes, which are so numerous that to list them with their physical constants and colors would have required several hundred additional pages. For that reason, the existing data are summarized in a separate chapter, which, while it does not constitute a thorough review of the thioindigo dyes, will, we hope, fill a gap in the chemical literature. The remaining chapters contain a critical review of the literature and a complete list of references to all condensed ring systems containing the thiophene nucleus and their respective derivatives. We shall be grateful for any omissions which are brought to our attention.

Various *nomenclature systems* have been used in the naming of condensed thiophene compounds. In the past few years, two new nomenclature systems have been proposed. One is the "oxa-aza-thia" system which systematically names oxygen, nitrogen, and sulfur heterocycles. The other system, which pertains only to sulfur heterocycles, uses the term "thiophene" as the basic root of all names. Both of these systems differ from that currently used by *Chemical Abstracts.*

In view of this confused state, both the A. C. S. Organo-Sulfur and the A. C. S. Heterocyclic Nomenclature subcommittees were consulted. There appeared to be a lack of agreement between these committees. For example, one committee suggested that 1-thiaindene be substituted for the common name, thianaphthene, while the other proposed the name, benzo-[*b*]thiophene. Since neither of these new systems had official sanction, it was decided to use *Chemical Abstracts* nomenclature, although the alternative names that have been used for each system are also listed. It should be pointed out that common names such as thianaphthene and thiophanthrene form the roots of many of the names of the complex ring systems of Chapters V to VIII, and changing the *Chemical Abstracts* nomenclature would have required the changing of all of these names without any assurance that the system we chose would eventually receive official approval. We are of the opinion that the systematic names, benzo[*b*]thiophene and 1-thiaindene, have some advantages over the common name, thianaphthene. However, we feel that one nomenclature system must be officially approved before the names now in use should be changed.

We thank the Socony-Vacuum Oil Company for permission to write this book and for the use of their library facilities. Dr. W. P. Hawthorne, by his painstaking proofreading and critical reviewing of this volume, has improved immeasurably its quality and organization. We are grateful to Dr. R. M. Dobres and Dr. C. M. Fontana of Socony-Vacuum Oil Company and to Dr. E. M. Crane of Eastman Kodak Company for their critical comments, and to Dr. R. O. Offenhauer and Mr. J. J. Dickert, Jr., for their help in the reading of proof. Hercules Powder Company furnished library facilities during the latter phases of the writing of this book and stenographic help in the typing of the manuscript.

Originally we had hoped to persuade someone familiar with thioindigo dyes to write Chapter III. This was not possible, but Mr. A. J. Johnson of E. I. du Pont de Nemours & Company kindly reviewed this chapter and advised us during the writing period. Mr. Johnson also provided the patent bibliography at the end of Chapter III and compiled Table I which deals with commercially available thioindigo dyes.

The writing of this book was facilitated by private communications from friends in this country and abroad. Sincere thanks for such help are due to Prof. F. G. Bordwell of Northwestern University, Prof. E. V. Brown of Fordham University, Prof. Frederick Challenger, The University, Leeds, England, Prof. O. Dann of the University of Erlangen, Germany, Prof. H. Gilman of Iowa State University, Prof. W. Herz of the University of Florida, and Prof. P. A. S. Smith of the University of Michigan.

The original draft of the book was completed in May, 1951; therefore, references 701 to 770 which appeared between that date and May 15, 1952, were inserted into the completed manuscript. Since it was not always possible to incorporate these references into the text, in some instances only a tabulation of the compounds and their physical constants has been given. With the exception of articles and patents that we may have overlooked, all references are included up to May 15, 1952.

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CONTENTS

I Factors Influencing Chemical Reactivity and Substitution of Thiophene Systems 1

- I. Introduction 1
- II. Electrophilic Substitution of Furan, Thiophene and Selenophene 2
- III. Electrophilic Substitution of Benzofuran, Thianaphthene, Selenonaphthene and the Thienothiophenes 4
- IV. Electrophilic Substitution of Dibenzofuran, Dibenzothiophene and Dibenzoselenophene 10
- V. Metalation of Thiophene Systems 14
- VI. Reactivity of the Sulfur Atom in Thiophene Systems 15

II Thianaphthene and Other Thiophene Compounds Containing One Carbocyclic Fused Ring 17

- Introduction 17
- A. Thianaphthene and Its Derivatives 17
- Nomenclature 18
- Occurrence of Thianaphthene in Nature 18
  - I. Preparation of Thianaphthene and Its Homologs 20
    - A. Thianaphthene 20
    - B. Monoalkylthianaphthenes 22
    - C. Dialkylthianaphthenes 24
    - D. Trialkylthianaphthenes 25
    - E. Arylthianaphthenes 26
  - II. Miscellaneous Reactions and Properties 29
  - III. The Hydrothianaphthenes 34
    - A. 2,3-Dihydrothianaphthene and Its Derivatives 34
    - B. 6,7-Dihydrothianaphthene 36
    - C. 4,5,6,7-Tetrahydrothianaphthene and Its Derivatives 37
  - IV. Halogen Derivatives 45
  - V. Nitrogen Derivatives 48
    - A. Nitrothianaphthenes 48
    - B. Aminothianaphthenes 51
    - C. Derivatives with Nitrogen in a Side Chain 58
  - VI. Hydroxythianaphthenes (Thianaphthenols or Thioindoxyls) 63
    - A. Tautomerism of 2- and 3-Hydroxythianaphthenes 64
    - B. Preparation of Hydroxythianaphthenes 66
      - 1. 2-Hydroxythianaphthenes 66
      - 2. 3-Hydroxythianaphthenes 67

II. Thianaphthene and Other Thiophene Compounds Containing One Carbocyclic Fused Ring (*continued*)

3. 4-Hydroxythianaphthenes ... 73
4. 5-Hydroxythianaphthenes ... 80
5. 6-Hydroxythianaphthenes ... 81
6. 7-Hydroxythianaphthenes ... 82
7. Di- and Trihydroxythianaphthenes ... 82

C. Reactions of Hydroxythianaphthenes ... 84
1. Reactions of the Enol Form ... 84
2. Reactions of the Keto Form ... 88

VII. Thianaphthenequinones ... 95
A. 2,3-Thianaphthenequinones ... 95
B. Benzenoid Thianaphthenequinones ... 102
1. 4,5-Thianaphthenequinones ... 102
2. 6,7-Thianaphthenequinones ... 104
3. 4,7-Thianaphthenequinones ... 104

VIII. Derivatives Containing Hydroxyl Groups in a Side Chain ... 107
IX. Carbonyl Derivatives ... 109
A. Thianaphthenecarboxaldehydes ... 109
B. Keto Derivatives of Thianaphthene ... 114
X. Thianaphthenecarboxylic Acids ... 124
A. Monocarboxylic Acids ... 124
B. 2,3-Thianaphthenedicarboxylic Acid and Its Derivatives ... 134
C. 3-Amino-2-thianaphthenecarboxylic Acid ... 137
D. 3-Hydroxy-2-thianaphthenecarboxylic Acid ... 138
E. Thianaphthenecarboxylic Acids with the Carboxyl Group in the Side Chain ... 141
XI. Thianaphthenesulfonic Acids and Thianaphthene Sulfides ... 153
XII. Mercury Derivatives ... 154
XIII. Thianaphthene 1-Oxides (Sulfoxides) ... 155
XIV. Thianaphthene 1-Dioxides (Sulfones) ... 156
A. Preparation ... 156
B. Reactions ... 159

B. Isothianaphthene and Its Derivatives ... 167
I. The Hydroisothianaphthenes ... 167
A. 1,3-Dihydroisothianaphthene (*o*-Xylylene Sulfide) ... 167
B. 6,7-Dihydro- and 4,5,6,7-Tetrahydroisothianaphthenes ... 168
II. Derivatives of Isothianaphthene ... 168

C. Miscellaneous Systems ... 172
I. Cyclopenta[*b*]thiophene ... 172
II. Cyclohepta[*b*]thiophene ... 173
III. 4,7-Endovinylenethianaphthene ... 173

III. Thioindigo and Related Dyes ... 175

Introduction ... 175
I. Nomenclature ... 178
II. Friedländer's Commercial Thioindigo Synthesis ... 181

III. Thioindigo and Related Dyes (*continued*)

III. Symmetrical Thioindigo Dyes . . . 181
- A. 2,2′-Bisthioindigos . . . 181
- B. 2,3′-Bisthioindigos (Thioindirubins) . . . 187
- C. 3,3′-Bisthioindigo (Isothioindigo) . . . 188

IV. Asymmetrical Thioindigos . . . 189
- A. Asymmetrical 2,2′-Thioindigoids . . . 189
- B. Asymmetrical Thioindirubins . . . 189
- C. Miscellaneous Thioindigoids and Related Materials . . . 190
- D. Condensation with Phenanthroquinones . . . 192

V. Thioindogenides and Anils of Thioindoxyls . . . 194

VI. Leucothioindigos (Thioindigo Whites) . . . 195

VII. Reactions of the Thioindigo Dyes . . . 197

VIII. Factors Affecting the Colors of Thioindigo Dyes . . . 199

IX. Indophenine and Related Dyes . . . 206

Scheme of Reactions Proving the Presence of the Dithienyl Nucleus . . 212

Index of References Pertaining to the Thioindigo Dyes Not in Text . . . 215

Index of References Pertaining to Naphthioindigos and Thioindigos Having More Complex Ring Systems Not Included in Preceding Index or Text . . . 215

United States Patents Pertaining to Thioindigos . . . 216

German Patents Pertaining to Thioindigos . . . 218

British Patents Pertaining to Thioindigos . . . 221

French Patents Pertaining to Thioindigos . . . 223

IV. Dibenzothiophene and Its Derivatives . . . 225

I. Introduction . . . 225

II. Dibenzothiophene . . . 226
- A. Nomenclature . . . 226
- B. Occurrence in Nature . . . 226
- C. Preparation . . . 227
  - 1. Historical . . . 227
  - 2. Cyclization of Biphenyls . . . 227
  - 3. Cyclization of Sulfur Compounds . . . 228
  - 4. Reduction of Oxides and Dioxides . . . 230
  - 5. Miscellaneous Methods . . . 231
- D. Reduction Reactions of Dibenzothiophene . . . 232
- E. Properties . . . 233
  - 1. Physical Properties . . . 233
  - 2. Toxicological Properties . . . 234
  - 3. Miscellaneous Properties . . . 235

III. Alkyl and Aryl Derivatives of Dibenzothiophene . . . 235

IV. Sulfoxides and Sulfones . . . 237

V. Halogen Derivatives . . . 241
- A. Chlorodibenzothiophenes . . . 241
- B. Bromodibenzothiophenes . . . 242
- C. Iododibenzothiophenes . . . 247

IV. Dibenzothiophene and Its Derivatives (*continued*)

- VI. Nitrogen Derivatives 248
  - A. Nitrodibenzothiophenes 248
  - B. Aminodibenzothiophenes 251
    - 1. Nuclear Amino Groups 251
    - 2. Side Chain Amino Groups 257
- VII. Hydroxl Derivatives of Dibenzothiophene 262
- VIII. Carbonyl Derivatives of Dibenzothiophene 268
  - A. Aldehydes 268
  - B. Ketones 268
    - 1. Carbonyl in Side Chain 268
    - 2. Carbonyl in Ring 271
- IX. Dibenzothiophenecarboxylic Acids 272
    - 1. Nuclear Carboxyl Group 272
    - 2. Carboxyl Group in Side Chain 274
- X. Sulfur Derivatives 276
- XI. Metallic Derivatives 278

V. Naphthothiophenes and Other Thiophene Compounds Containing Two Carbocyclic Fused Rings 283

- I. Introduction 283
- II. Thiophanthrene Ring Systems 284
  - A. Thiophanthrene 284
  - B. Alkyl and Aryl Derivatives of Thiophanthrene 284
  - C. Acids of Thiophanthrene 286
  - D. 3-Hydroxythiophanthrene and Derivatives 286
  - E. 2,3-Thiophanthraquinone and Derivatives 288
  - F. 4,9-Thiophanthraquinone and Derivatives 288
- III. Naphtho[2,3-*c*]thiophene Ring Systems 296
- IV. Naphtho[1,2-*b*]thiophene Ring Systems 296
  - A. Naphtho[1,2-*b*]thiophene 296
  - B. Alkyl Derivatives of Naphtho[1,2-*b*]thiophene 297
  - C. 3-Hydroxynaphtho[1,2-*b*]thiophene and Derivatives 298
  - D. 2,3-Naphtho[1,2-*b*]thiophenequinone and Derivatives 299
- V. Naphtho[2,1-*b*]thiophene Ring Systems 302
  - A. Naphtho[2,1-*b*]thiophene 302
  - B. Alkyl Derivatives of Naphtho[2,1-*b*]thiophene 303
  - C. Acids of Naphtho[2,1-*b*]thiophene 303
  - D. 1-Hydroxynaphtho[2,1-*b*]thiophenes and Derivatives 304
  - E. 1,2-Naphtho[2,1-*b*]thiophenequinone and Derivatives 307
- VI. 2*H*-Naphtho[1,8]thiophene 310
- VII. Naphtho[1,2-*c*]thiophene 311
- VIII. Miscellaneous Three-Ring Systems Containing One Thiophene Ring 311
  - A. 8*H*-Indeno[2,1-*b*]thiophene Ring System 311
  - B. 3*H*-Cyclopenta[*b*]thianaphthene Ring System 312
  - C. 8*H*-Cyclopenta[*g*]thianaphthene Ring System 312
  - D. Cycloocta[*g*]thianaphthene Ring System 313

VI. Thiophene Systems Containing Three or More Carbocyclic Fused Rings 315

- I. Introduction 315
- II. Four Ring Systems 315
  - A. 6*H*-Indeno[2,1-*f*]thianaphthene 315
  - B. Acenaphtheno[1,2-*c*]thiophene 316
  - C. Benzo[*b*]thiophanthrene 316
    - 1. Benzo[*b*]thiophanthrene 317
    - 2. 6,11-Benzo[*b*]thiophanthraquinone and Derivatives 318
  - D. Benzo[*g*]thiophanthrene 323
  - E. Benzo[*i*]thiophanthrene 327
  - F. Naphtho[2,1-*b*]thianaphthene 328
  - G. Anthra[2,3-*b*]thiophene 331
  - H. Anthra[1,2-*b*]thiophene 331
  - I. Anthra[2,1-*b*]thiophene 333
  - J. Phenanthro[2,3-*b*]thiophene 334
  - K. Phenanthro[3,4-*b*]thiophene 335
  - L. Phenanthro[4,3-*b*]thiophene 336
  - M. Phenanthro[9,10-*b*]thiophene 338
  - N. Phenanthro[9,10-*c*]thiophene 338
  - O. 6,*H*-Anthra[1,9-*bc*]thiophene 340
  - P. 7*H*-Benzo[*ef*]thiophanthrene 341
  - Q. 7*H*-Benzo[*jk*]thiophanthrene 342
  - R. 7*H*-Naphth[1,8-*ef*]isothianaphthene 343
- III. Five Ring Systems 343
  - A. Diindeno[1,2-*b*,2′,1′-*d*]thiophene 343
  - B. Diindeno[2,1-*b*,1′,2′-*d*]thiophene 344
  - C. 7*H*-Benz[6,7]indeno[1,2-*b*]thianaphthene 345
  - D. 12*H*-Benz[4,5]indeno[1,2-*e*]thianaphthene 345
  - E. Dibenzo[*b*,*h*]thiophanthrene 346
  - F. Dinaphtho[2,3,2′,3′]thiophene 347
  - G. Dibenzo[*b*,*i*]thiophanthrene and Dibenzo[*b*,*g*]thiophanthrene 348
  - H. Dinaphtho[2,1,2′,3′]thiophene 348
  - I. Dinaphtho[1,2,2′,1′]thiophene 349
  - J. Dinaphtho[2,1,1′,2′]thiophene 349
  - K. Phenanthro[3,4-*b*]thianaphthene 350
  - L. 7*H*-Dibenzo[*b*,*jk*]thiophanthrene and 7*H*-Dibenzo[*b*,*ef*]thiophanthrene 350
  - M. Anthra[2,1,9-*cde*]thianaphthene 351
  - N. Pyreno[2,1-*b*]thiophene 351
- IV. Six Ring Systems 352
  - A. 5*H*-Naphth[1′,2′,2,3]indeno[4,5-*b*]thianaphthene 352
  - B. 7*H*-Naphth[1′,2′,6,7]indeno[1,2-*b*]thianaphthene 352
  - C. Acephenanthryleno[7,8-*g*]thianaphthene 353
- V. Seven Ring Systems 354
  - A. Diacenaphtho[1,2-*b*,1′,2′-*d*]thiophene 354
- VI. Eight Ring Systems 354
  - A. Flavophene 354

VII. Condensed Thiophenes Containing O,S, and Hg Ring Systems...... 357

Introduction........ 357
I. Furan Ring Systems... 357
II. Pyran Ring Systems 360
  A. C_4S-C_5O Systems 360
  B. $C_4S-C_5O-C_6$ Systems 361
  C. $C_4S-C_5O-C_5O-C_6-C_6$ Systems 365
  D. $C_4S-C_5O-C_6-C_6-C_6$ Systems 366
III. Miscellaneous O, and O,S Ring Systems 367
  A. $C_3O_2-C_4S-C_6$ Systems 367
  B. $C_4S-C_4O_2$ Systems 368
  C. C_2OS-C_4S and $C_2S_2-C_4S$ Systems 368
  D. $C_2OS_2-C_4S$ Systems 370
  E. $C_4S-C_6-C_6-C_8OS$ Systems 371
  F. Miscellaneous Macro Ring Systems 371
IV. Multiple Thiophene Ring Systems 372
  A. C_4S-C_4S Systems (Thiophthenes) 372
  B. $C_4S-C_4S-C_6$ Systems 381
  C. $C_4S-C_4S-C_6-C_6$ Systems 385
  D. $C_4S-C_4S-C_6-C_6-C_6$ Systems 389
  E. $C_4S-C_4S-C_6-C_6-C_6-C_6$ Systems 390
  F. $C_4S-C_4S-C_6-C_6-C_6-C_6-C_6-C_6$ Systems 391
  G. $C_4S-C_4S-C_4S-C_6-C_6$ Systems 393
  H. $C_4S-C_4S-C_4S-C_6-C_6-C_6-C_6$ Systems 393
V. Thiapyran Ring Systems 394
  A. C_4S-C_5S Systems 394
  B. $C_4S-C_5S-C_6$ Systems 395
  C. $C_4S-C_4S-C_5S$ Systems 396
  D. $C_4S-C_4S-C_5S-C_6-C_6$ Systems 398
  E. $C_4S-C_5S-C_5S-C_6-C_6$ Systems 399
  F. A $C_4S-C_5S-(C_6)_{10}$ System 400
VI. Mercury Ring Systems 401
  A. $C_4S-C_4S-C_4Hg_2$ Systems 401
  B. $C_4S-C_4S-C_4S_2Hg_2$ Systems 401
  C. $C_4S-C_4S-C_4S-C_4S-C_8S_4Hg_2$ Systems 402

VIII. Condensed Thiophene Compounds Containing Nitrogen Ring Systems 403

Introduction 403
I. Five-Membered Nitrogen Ring Systems 404
  A. Triazole Ring Systems 404
  B. Diazole Ring Systems 404
  C. Pyrrole Ring Systems 408
II. Diazine Ring Systems 420
  A. Pyridazine Ring Systems (1,2-Diazines) 420
  B. Pyrimidines (1,3-Diazines) 421
  C. Pyrazines (1,4-Diazines) 422

VIII. Condensed Thiophene Compounds Containing Nitrogen Ring Systems (*continued*)

III. Pyridine Ring Systems 427
- A. $C_4S–C_5N$ Systems 427
- B. $C_4S–C_5N–C_6$ Systems 432
- C. $C_4S–C_5N–C_6–C_6$ Systems 435
- D. $C_4S–C_5–C_5N–C_6–C_6$ Systems 437
- E. $C_4S–C_5N–C_6–C_6–C_6$ Systems 438
- F. $C_4S–C_5N–C_6–C_6–C_6–C_6$ Systems 438
- G. $C_4S–C_4S–C_5N–C_6–C_6$ Systems 439
- H. $C_4S–C_5N–C_5N–C_6$ Systems 439

IV. N,S and N,O Ring Systems 440
- A. Thiazoles Containing $C_4S–C_3NS–C_6$ Systems 440
- B. *p*-Thiazines Containing $C_4S–C_4NS–C_6$ Systems 442
- C. Thieno[2,3-*d*]oxazole 443
- D. *m*-Oxazines Containing $C_4S–C_4NO–C_6$ Systems 443

V. Macro Nitrogen Ring Systems 445
- A. $C_4S–C_6–C_6–C_6N$ Systems 445
- B. $C_4S–C_4S–C_4S–C_4S–C_4N–C_4N–C_4N–C_4N–C_8N_8$ 445
- C. $C_4S–C_4S–C_4S–C_4S–C_4N–C_4N–C_6–C_6–C_{10}S_4$ 446
- D. Macro Ring Systems of Doubtful Structure 446

IX. Condensed Selenophene and Tellurophene Systems 447

Introduction 447

I. Carbocyclic Condensed Selenophene Systems 447
- A. Selenonaphthene 447
- B. Isoselenonaphthene 451
- C. Dibenzoselenophene 455
- D. Anthraselenophene 457

II. Heterocyclic Condensed Selenophene Systems 458
- A. The Isomeric Selenophthenes 458
- B. Seleno[*lmn*][4,7]phenanthroline 459
- C. Selenonaphtheno[4,5-*b*]quinoxaline 459

III. Condensed Tellurophene Systems 460
- A. Telluronaphthene 460
- B. Dibenzotellurophene 460

Bibliography 463

Patent Bibliography 479

Ring Index 497

Subject Index 501

CHAPTER I

Factors Influencing Chemical Reactivity and Substitution of Thiophene Systems

I. Introduction

Many investigators have attempted to relate the chemistry of resonating heterocyclic systems to that of benzene and its homologs. This has been especially true of thiophene compounds, since their reactions often appear to be identical to those of the corresponding benzene systems. This surface similarity between benzene and thiophene has caused a number of the early investigators to minimize and sometimes to ignore completely the influence of the sulfur atom on the chemistry of the entire molecule. For example, even in cases where the thiophene ring is substituted with powerful electron-withdrawing groups (*nitro*, carboxyl) in the 2-position, the directing effect of the sulfur is usually the major one and substitution at the 5-position (para to 2-position) predominates.

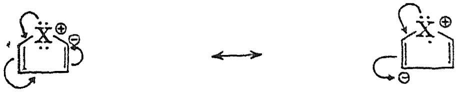
It is now generally recognized that the influence of the sulfur atom on the chemistry of thiophene systems is extremely significant. These effects and their influences on the various orientations in thiophene systems are discussed in this chapter. A discussion of the effect of oxygen and selenium on their respective heterocyclic systems is also included and compounds in these systems are compared with the corresponding thiophene analogs. It was found that such a comparison is helpful in explaining many of the orientation effects present in thiophene compounds, since they usually fall in between those of the furan and selenophene systems.

In many cases, certain orientations occurring in these systems were not discussed by the original investigators. Wherever possible, an attempt has been made to present interpretations for these substitutions in terms of modern concepts.

Finally, it must be emphasized that the following discussion is nonmathematical. It is an attempt to review those factors which influence the reactivity and orientation of thiophene systems so that many of the specific reactions discussed in subsequent chapters can be classified systematically. This classification should be helpful in predicting the course of reactions involving thiophene systems.

II. Electrophilic Substitution of Furan, Thiophene and Selenophene

The electrophilic substitution (*i.e.*, substitution by an electron-seeking group) of furan, thiophene, and selenophene occurs preferentially at the 2-position. The only reported case in which an appreciable amount of 3-substitution occurs is in the alkylation and polymerization of thiophene (603,699,700). This preponderant 2-substitution is difficult to explain qualitatively, since if resonating structures I and II are assumed to contribute equally, then equal ease of substitution in the 2- and 3-positions is expected.

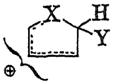


(I) (II)

X = O, S, or Se

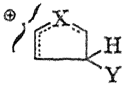
Several investigators have considered the 2-substitution of pyrrole. Since the same theories used to explain the substitution of pyrrole can also be adapted to the above systems, they are presented here.

Remick (686,686A) has stated that 2-substitution would be predicted, since the electron displacement putting a negative charge at the 2-position should occur more easily due to the more extended conjugation that occurs in I. Schomaker and Pauling (688) have pointed out that the smaller charge separation in structure I would favor this form over II. Dewar (689), using the molecular orbital theory, has advanced the following arguments to show that the transition state favoring 2-substitution (III) is more stable than the transition state favoring 3-substitution (IV).



(III)

Y^+ = electrophilic group



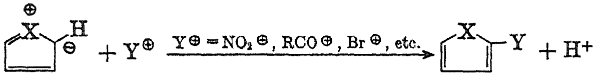
(IV)

In any conjugated system where one atom has an abnormally high electron affinity, the electronic symmetry is less than in a similar system where all atoms are alike. This odd atom acquires excess electronic charge and the bonds attached to it become weakened, which, in turn, results in a decrease in stability of the conjugated system. Now if the odd atom is at the end of a conjugated system as in III, only one bond is weakened, while if it is in the middle of such a system (IV) two bonds are weakened. Therefore, transition state III is the more stable and 2-substitution predominates.

Although all of the explanations that have been presented up to now can account for the preferential reactivity of the 2-position of thiophene toward electrophilic substitution, none of them explains satisfactorily why the 2-position is preferentially substituted in benzofuran (544), as opposed to the 3-position of thianaphthene.

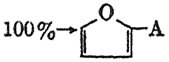
This indicates that effects other than those predicted by either resonance or molecular orbital concepts should be considered. For example, how does the electronegativity of the heteroatom influence further substitution and what effect will be caused if there is initially a coordination between the electronegative heteroatom and a positively charged material such as a proton? Both of these phenomena should deactivate the heterocycle with respect to an electrophilic attack, and in the case of the noncondensed systems they would favor 3-substitution. Since these effects appear to be more important in the condensed systems, a further consideration of them will be deferred until the substitution of these systems is discussed.

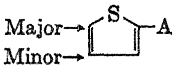
The electrophilic substitution of furan, thiophene, or selenophene requires an electrophilic group (Y^+) to react with the heterocycle in its activated form (I). The proximity of the electrophilic group can induce the formation of I (Electromeric effect, E) (686). The ease with which these heteroatoms permit a pair of electrons to enter into conjugation with a resonating system (+E effect) is greatest with oxygen and least with selenium. Therefore, it is reasonable to expect that the oxygen atom in furan would have the greatest activating influence and selenium the smallest.

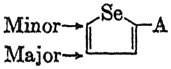


(I)

This can be demonstrated by considering the electrophilic substitution of these heterocyclic compounds containing a ring-deactivating group, A (nitro, carboxyl, etc.), in the 2-position. In furan, the influence of the O is so great that in spite of the deactivating influence of A, substitution still occurs almost entirely at the 5-position (692). Again an exception is found in the alkylation reaction. Furfural reacts with isopropyl chloride to yield the 4-isopropyl derivative (687). In thiophene, the 5-position is deactivated sufficiently to allow some substitution to occur meta to A.

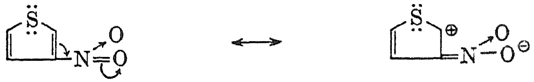






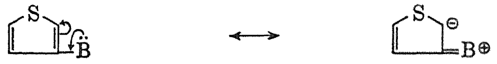
With the —SO_2Cl group in the 2-position, meta substitution actually predominates (471,700). In selenophene, the dominant directive influence is exerted by A (691,700).

In cases where A is in the 3-position, it should exert the greatest deactivating effect on the 2- and 4-positions. This is illustrated for the 2-position of 3-nitrothiophene. Substitution in these cases should occur exclusively at the 5-position (700), since this position is the least deactivated and is, of course, still activated by the heteroatom.



When these systems are substituted in the 2-position by an electron-donating group, B, the directive influences are additive and substitution occurs entirely at the 5-position.

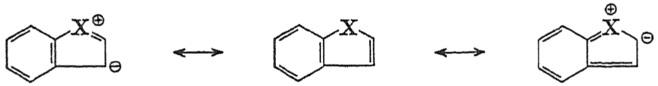
When B is in the 3-position, substitution occurs predominantly at the 2-position, although some substitution occurs at the 5-position (700,623). This predominant 2-substitution is due to the added effects of B and the heteroatoms. When B is an alkyl group, a consideration of both inductive and hyperconjugation effects also lead to the above conclusions.



III. Electrophilic Substitution of Benzofuran, Thianaphthene, Selenonaphthene and the Thienothiophenes

The factors involved in the substitution of benzofuran, thianaphthene, and selenonaphthene appear to be more complex than in the noncondensed systems. Benzofuran is substituted almost exclusively at the 2-position (544), while the substitution of thianaphthene occurs predominantly at the 3-position. With some reactions, however, considerable substitution occurs at the 2-position. The orientation in selenonaphthene has not been studied. On the basis of some of the effects that are discussed in this section, it would be predicted that electrophilic substitution of selenonaphthene should occur almost exclusively at the 3-position.

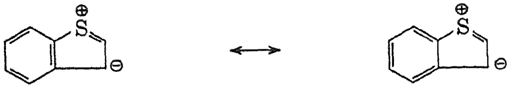
Resonance considerations of the condensed system I lead to the prediction that, although the 2- and 3-positions are activated, electrophilic substitution will occur preferentially at the 3-position. This directive influence of the heteroatoms in condensed systems stands in contrast to that in the noncondensed systems, in which the 2-position is preferentially activated. This change in predicted orientation may be explained by a consideration of structures II and III. The formation of III requires a



(II) (I) (III)

X = O, S, or Se

resonance interaction between the benzene and the heterocyclic ring which is not necessary for the formation of II. Thus, there are two ionic excited forms, II and IIA,



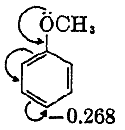
(II) (IIA)

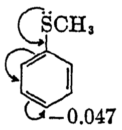
which have a negative charge in the 3-position and only one form, III, which has a negative charge in the 2-position. The additional resonance in structures such as II has been used previously as an explanation for β-substitution in indole (688).

Although the electrophilic substitution of thianaphthene occurs predominantly at the 3-position, appreciable yields of the 2-substituted product have been obtained (544). Substitution of benzofuran occurs almost exclusively at the 2-position (544,693,694). The nitration of benzofuran is also reported to yield a minor amount of an isomeric nitro compound which may be 5-nitrobenzofuran.

These differences in orientation between benzofuran and thianaphthene have been discussed by Farrar and Levine (544). They concluded that these differences are related to the relative electronegativities of the oxygen and sulfur atoms and since oxygen is more electronegative than sulfur (681), the unshared electrons around the oxygen in furan should be held more tightly than those by the sulfur in thiophene. This, they contend, would lead to 2-substitution in benzofuran and stabilization of the furan nucleus.

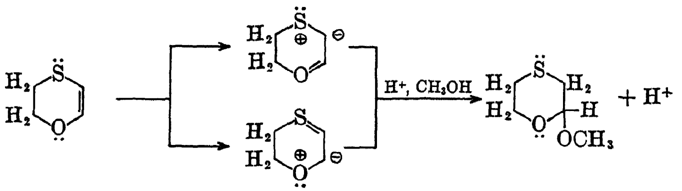
Although it seems probable that the electronegativity of the heteroatoms does contribute to the differences in the orientation of benzofuran and thianaphthene, it should be pointed out that when the heteroatom is part of a resonating system, the order of electron release ($+E$ effect) for atoms of group VI is: OR > SR > SeR (686). With the halogens the order is: F > Cl > Br > I and it is stated that despite the fact that fluorine has the firmest grip on its unshared electrons, it releases them most easily for double bond formation. A possible reason for this apparently anomalous tendency is that the larger atoms find it more difficult to increase their covalences, as they must if they are to release their electrons to a resonating system. A comparison of the Hammett σ values for the *p*-positions of anisole and thioanisole support the conclusion that the electromeric release of oxygen is greater than that of sulfur (680,769). These σ values are a



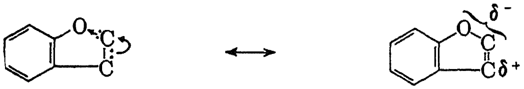


measure of the electron density at the designated position and thus are in this case an indirect measure of the electron-releasing ability of the respective heteroatoms.

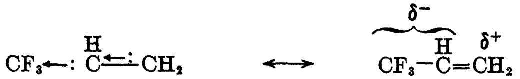
Recently reported data by Parham, Gordon, and Swalen (751) on the acid catalyzed addition of methanol to *p*-oxathiene (IV) corroborate this



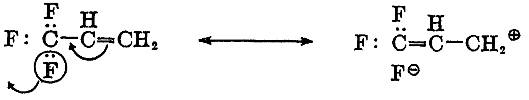
conclusion. Resonance modifications of IV are shown by structures IVA and IVB, IVA occurring when there is a release of oxygen electrons and IVB, resulting from a release of sulfur electrons. The first step in this reaction involves the attack of the *p*-oxathiene by a positive ion. Since only 2-methoxy-*p*-oxathiane is formed, the intermediate step must have involved an electrophilic attack on IVA, indicating that the electrons are released more readily by oxygen than by sulfur. This same conclusion was also reached by Baddely (751A) from consideration of various reactions involving oxygen and sulfur systems. The electronegativity effect considered by Farrar and Levine would favor 2-substitution in benzofuran systems. However, it should be considered in combination with the electromeric effect. If we first consider the effect related to the electronegativity of the heteroatoms, it seems reasonable to expect that the C—O bond in benzofuran would be more permanently polarized (static inductive effect, $-I_s$) (686) than the C—S bond in thianaphthene. This displacement of electrons toward the heteroatom should cause a polarization of the adjacent double bond, displacing the π (bond-forming) electrons nearer to the α-carbon atom. This effect is ring-deactivating and would favor 2- rather than 3-substitution.


(1)

There may be some objections to the type of shift depicted in (1), since it has not been definitely established that such a shift can be caused by a neutral atom or molecule. Even in the case of trifluoromethylethylene, where such a shift appears to take place (690), a transfer of electrons plus an ionization of one of the fluoro groups has been postulated as a possible alternative (770).


(2)

$$CF_3 \leftarrow : \overset{H}{C} \leftarrow CH_2 \longleftrightarrow CF_3-\overset{H}{C}=CH_2 \quad \delta^- \ \delta^+$$

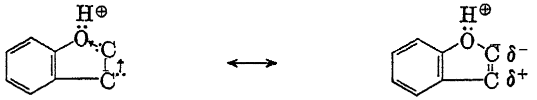

(3)

$$F:\underset{F}{\overset{F}{C}}-\overset{H}{C}=CH_2 \longleftrightarrow F:\overset{F}{C}=\overset{H}{C}-CH_2^{\oplus} \quad F^{\ominus}$$

Equation 2 shows the very electronegative CF_3— group attracting a pair of electrons, which in turn causes a polarization of the adjacent double bond. Hydrogen halides in the absence of peroxides add sluggishly to this system, with the positive hydrogen ion going to the central carbon atom. This shows that the charge distribution depicted in (2) is correct. This shift of electrons is similar to the one shown in (1).

The same charge distribution is achieved in (3), but in this case there is an ionization of a fluoro atom which allows a transfer of electrons to occur. This transfer of electrons cannot occur in benzofuran.

Objections to the shift shown in (1) may be circumvented by postulating an initial coordination between the oxygen and a positively charged material such as a proton. This would produce a shift in electrons similar to that shown in (1). This distortion of electrons would favor the 2-position



with respect to electrophilic substitution and it would also tend to decrease the aromaticity of benzofuran and make it behave more like an olefin. The experimental fact that bromine adds to benzofuran to form the 2,3-dibromide agrees with this conclusion.

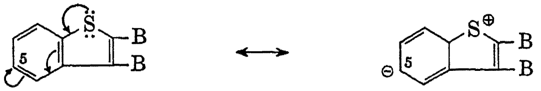
The ability of atoms of group VI to coordinate with a positive ion should be: O > S > Se. Also this ability to coordinate with a positive ion should be greater for the condensed systems, since their heteroatom electrons are more available for coordination than are those in the noncondensed systems. This point is discussed more fully in section VI.

The fact that the electrophilic substitution of benzofuran occurs almost exclusively at the 2-position indicates that there must be considerable deactivation of the 3-position to offset its enhanced activation due to additional resonance structures. The 2-position is also deactivated, but to a lesser extent. This deactivation cannot be the dominant effect, for if it were, benzofuran would behave like an aromatic system substituted with a ring-deactivating group, and it is well known that the reactivity of furan systems is in many ways comparable to benzene systems having ring-activating groups. It therefore appears that the algebraic sum of these activating and deactivating effects make the 2-position more negative than the 3-position and consequently the 2-position is favored in electrophilic substitution reactions.

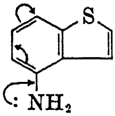
The same effects probably occur in thianaphthene, but in this case the 3-position is not deactivated sufficiently to allow a major amount of 2-substitution. However, in spite of the larger deactivation of benzofuran with respect to thianaphthene, it is still possible that benzofuran is more active than thianaphthene due to the initially larger activating effect ($+E$) of the oxygen. It would be interesting to run some competitive electrophilic substitutions of both of these materials so that this point could be determined.

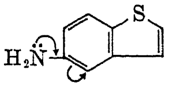
Orientation studies of selenonaphthene have not been reported. However, in this case there should be very little deactivation of the 3-position and consequently 3-substitution would be expected almost exclusively.

The presence of an ortho-para directing group in either the 2- or 3-position of thianaphthene directs further electrophilic substitution to the adjacent position in the thiophene ring. The position of the third substitution, which must take place on the benzene nucleus, has not been established. On the basis of the following resonating structures and a consideration of the arguments that will be used to account for 2-substitution in dibenzothiophene, it appears most likely that this substitution will occur predominantly at the 5-position.



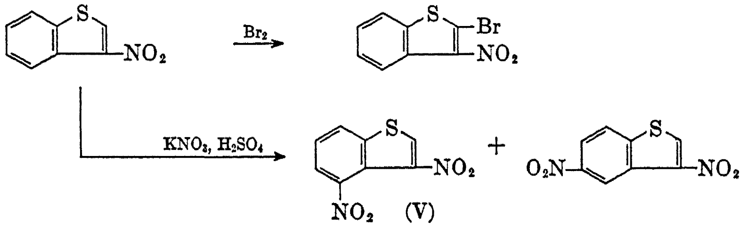
The orientation in thianaphthene, when a ring-activating group is on the benzene nucleus, has been studied only with 4-amino and 5-aminothianaphthene. Substitution occurs at the 7- and 4-positions, respectively.





With the amino group in the 4-position, some 5-substitution might also have been expected.

The substitution of thianaphthene having an electron-withdrawing group has been studied only with 3-nitrothianaphthene (222). Bromination occurs at the 2-position (P-598), but nitration occurs in the benzene nucleus at the 4- and 5-positions (222). Why these different orientations

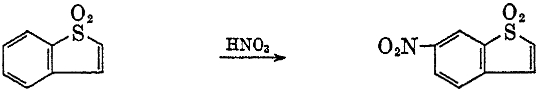


Major Minor

occur is not clear. However, it does suggest that consideration of only the electronic distribution of the nucleus is an over-simplification and that a knowledge of the nature of the electrophilic agent along with the electronic distribution of the nucleus may be necessary for an accurate explanation of some orientation effects.

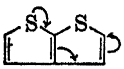
It is interesting that the further nitration of V is reported to occur at the 7 position (222). This is rather unusual since it involves substitution para to a nitro group, although ortho and para substitution to a nitro group is probably involved in the formation of some of the isomers isolated from the nitration of toluene (695).

The oxidation of thianaphthene with hydrogen peroxide yields thianaphthene 1-dioxide. The reactions of this molecule bear no resemblance to those of thianaphthene. The dioxide behaves primarily like a vinyl sulfone. The only nuclear substitution of thianaphthene 1-dioxide that has been reported is nitration which occurs at the 6-position (100).

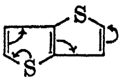


Since the electronegative sulfone group exerts a primary deactivation effect at the 5- and 7-position, substitution would be expected to occur at either the 4- or 6-positions. The effect of this internal sulfonyl group on substitution is discussed more thoroughly under the substitution of dibenzothiophene 5-dioxide (see section IV following).

The position at which the electrophilic substitution of thieno(2,3-*b*)-thiophene (VI) and thieno(3,2-*b*)thiophene (VII) occurs have been established recently (757). In each case, orientation to the 2-position occurs



(VI)



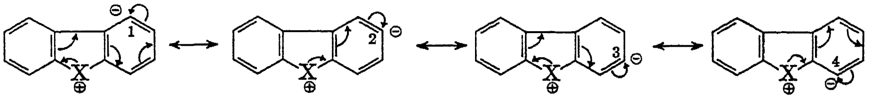
(VII)

This indicates a reasonance interaction between the two rings. In the other 2-ring systems, which involve a benzene ring, such an interaction was not favored, since it precluded Kekule resonance, and would lead to systems having fewer resonance structures. In the thienothiophenes the structures having a double bond common to both rings are most important and, consequently, a resonance interaction between the rings does not lead to fewer structures. Thus, the same arguments advanced for 2-substitution in thiophene also account for substitution in the thienothiophenes. The reactions involved in establishing the orientation of these thienothiophenes are discussed in chapter VII.

IV. Electrophilic Substitution of Dibenzofuran, Dibenzothiophene and Dibenzoselenophene

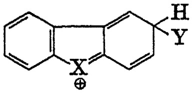
The electrophilic substitution of dibenzofuran and dibenzothiophene normally occurs at the 2-position. Although there are very few cases where the position of substitution in the dibenzoselenophene nucleus is known, it appears that here also the 2-position is substituted preferentially (38, 39,706). Recent ultraviolet absorption data indicate that dibenzoselenophene is nitrated in the 2-position (773).

All four positions of the benzenoid ring in these systems can be activated as is shown by the accompanying ionic excited structures. Structures I and III involve resonance interactions with both benzene rings, while in structures II and IV one benzene ring maintains its Kekulé structure. On this basis it would be predicted that substitution would occur at either the 2- or 4-positions.



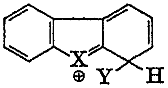
(I) (II) (III) (IV)

The reasons for 2-substitution rather than 4-substitution are more complex. Preferred 4-substitution might have been expected, since this structure involves a more favorable charge separation (688) and a more extended conjugation (686,686A). However, if we consider the transition states of II and IV (IIA and IVA), it is seen that structure IIA involves a p-quinoid system which is inherently more stable than the o-quinoid system in IVA (698).



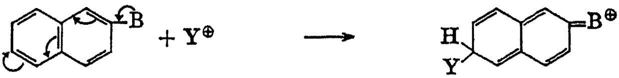
(IIA)

Y^+ = electrophilic group



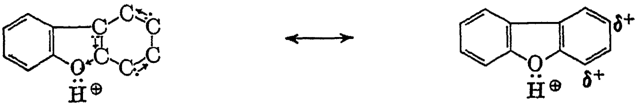
(IVA)

Some evidence in support of this theory can be found by considering the further substitution of naphthalene when it is substituted in the β-position by an ortho-para directing group (696). When the substitution takes place in the other ring it usually occurs first at the 6-position, which involves a p-quinoid structure in the transition state.



The only other position involved in the electrophilic substitution of the unsubstituted dibenzothiophene is the 4-position. Substitution in this position occurs in the acylation of dibenzothiophene where the 2- and a minor amount of the 4-isomer have been isolated (70,71). Isomer formation in other electrophilic substitutions is not reported, but certainly would be expected if the observations on the acylation reaction are correct.

The only anomalous electrophilic substitution of these heterocycles occurs in the nitration of dibenzofuran, where substitution occurs at the 3-position (655). However, as has been mentioned previously, oxygen can readily coordinate with a positive ion and for the oxygen systems that have been discussed, this coordination ability would be greatest for dibenzofuran (see section VI for explanation of latter statement). In any nitrating mixture a high concentration of protons is present and it may be that in this case the nitronium ion (NO_2^+) is attacking a coordinated dibenzofuran. Initial coordination with a proton would cause the following shift of electrons. This would deactivate preferentially the 2- and 4-

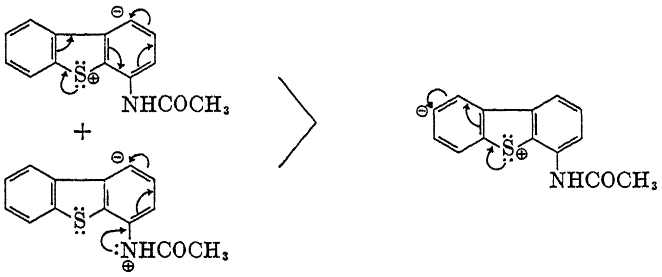


positions and on the basis of orientation studies of the sulfoxides and sulfones of dibenzothiophene, substitution would be expected at the 3-position. The nitration of dibenzothiophene proceeds normally and apparently exclusively at the 2-position.

When dibenzothiophene is substituted with a ring-deactivating group, substitution occurs in the 8-position of the unsubstituted ring. For example, the bromination of 2-nitrodibenzothiophene and the nitration of 2-bromodibenzothiophene yield 2-nitro-8-bromodibenzothiophene. Also, bromination and nitration yield the 2,8-disubstituted derivatives.

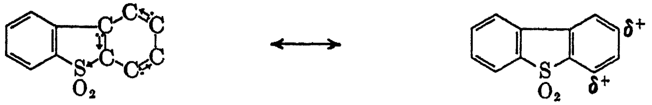
The effect of ring-activating groups on further substitution has not been established clearly. There are data, however, that indicate that electron-donating groups, such as the methoxyl or acetamido group, cause further substitution to take place in the substituted ring. For example, both the bromination of 4-acetamidodibenzothiophene and the nitration of 4-methoxydibenzothiophene occur predominantly at the 1-position (231,240). The nitration of 4-methoxydibenzothiophene also yields a small amount of the 3,4-isomer. The bromination of 2-acetamidodibenzothiophene yields the 2,3-isomer and cyclization of 4-(2′-dibenzothienyl)-butyric acid likewise occurs at the 3-position (526,77). Similar orientation effects have been observed in the dibenzofuran series.

On the surface it appears that the directing influence of these groups is greater than that of the heteroatom. This is not necessarily true, since, as has been shown, these heteroatoms can activate all four positions of the aromatic ring and the heteroatom will augment the directive influence of a specific group. Therefore, substitution of 4-acetamidodibenzothiophene at the 1-position merely means that the activation caused by the acetamido group is greater than the difference in activation of the 8- and 1-positions due to the heteroatom. These effects are illustrated in the accompanying formulas.

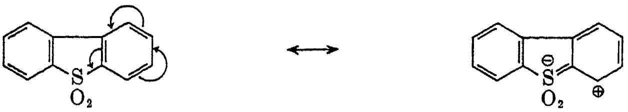


The substitution of a dibenzothiophene nucleus with activating groups in the 1-position has not been studied. It appears that 2-substitution should be favored, although some 4-substitution is also a distinct possibility. It would be interesting to investigate the electrophilic substitution of 2-alkyldibenzothiophenes to determine whether the activating effect of the alkyl group is sufficiently great to cause further substitution to occur in the substituted ring. The acylation of 2-alkyl-substituted dibenzofuran systems is reported to occur at the 8-position (613).

The oxides and dioxides of dibenzothiophene are substituted in the 3-position. The sulfoxides and sulfones behave like meta-directing groups in that they can withdraw electrons from the ring causing ring stabilization (135). As can be seen from the following structure, the 1- and 3-positions are the least deactivated.



The above structures merely show the displacement of the π electrons caused by the inductive effect of the sulfonyl group. It is conceivable that new bonds can also be formed through an electromeric mechanism leading to an expanded valence shell of the sulfur atom. As in the previous case, the 2- and 4-positions are deactivated preferentially. Disub-



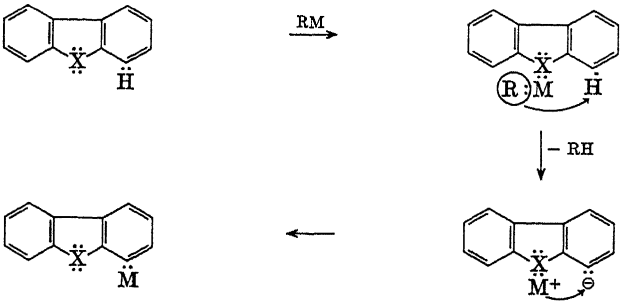
stitution of these oxides by electron-withdrawing groups yields the 3,6-derivatives.

V. Metalation of Thiophene Systems

The monometalation of furan and thiophene ring systems with alkaline earth metals occurs almost exclusively at the position adjacent to the heteroatom. An exception occurs with phenylcalcium iodide which metalates dibenzothiophene at the 3-position (232). The metalation of dibenzofuran with phenylcalcium iodide occurs at the normal 4-position.

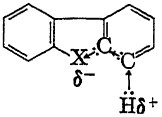
Roberts and Curtin (697) have pointed out that in nuclear metalation reactions, it appears that the ease of metalation is determined by the magnitude of the inductive effect of the heteroatom or hetero group. Thus, the metalation of furan systems should occur more easily than that of the corresponding thiophene systems, since oxygen is more electronegative than sulfur. This is actually the case, as has been shown by competitive metalation reactions of dibenzofuran and dibenzothiophene in which the dibenzofuran is preferentially metalated (234,237).

The following type of mechanism was advanced to explain why α-orientation occurred and how the inductive effect determines the rate of reaction. The initial step involves a coordination of the metallic atom



with an unshared pair of electrons of the heteroatom. This is followed by removal of the α-hydrogen by the anion of the metalating agent and migration of the cation to the α-position.

It is readily apparent that the electronegativity of the heteroatom will determine the acidity of the α-hydrogen, since the degree of polarization of C—H bond will be related to the electronegativity of the heteroatom.



As the acidity of this hydrogen increases, it becomes increasingly easy for it to be removed by the negative anion.

Additional reasons in favor of an initial coordination are:

1. It would weaken the carbon-metal bond and thus facilitate the transfer of the anion to the nucleus.
2. It would enhance the inductive effect of the electron-withdrawing heteroatom.
3. It would decrease the tendency for the electrons of the heteroatom to enter into resonance with the ring. This resonance would tend to decrease the acidity of the nuclear hydrogens.

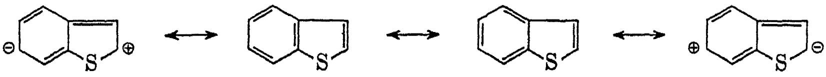
Although there are several instances where this mechanism fails to account for the observed orientation, it does satisfactorily explain the overwhelming majority of nuclear metalation reactions.

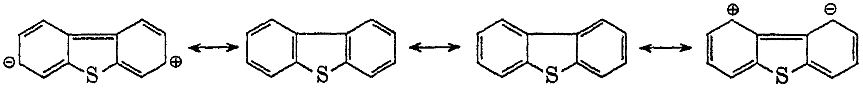
Gilman and Esmay (735) have postulated a similar mechanism to account for the products obtained from the metalation of dibenzothiophene 5-oxide. This reaction is discussed in detail in section XI of Chapter IV.

VI. Reactivity of the Sulfur Atom in Thiophene Systems

It has become increasingly evident that the chemical reactivity of sulfur in a C—S—C linkage is greatly modified in resonating systems. For example, the sulfones, sulfoxides, and dihalides of aliphatic sulfides form readily, while those of thiophene itself have never been isolated in the pure state. However, Backer and his coworkers (701) have recently reported that stable sulfones can be produced from a variety of substituted alkylthiophenes. Since the ease of coordination of the sulfur is dependent on the availability of its free electrons, this indicates that in resonating systems the electron density around the sulfur is less than in nonresonating systems. It is also apparent that the electron densities around the sulfur must vary with different resonating systems, since the sulfones of thianaphthene and dibenzothiophene and their derivatives and the dichloride of dibenzothiophene can be prepared readily.

Charles and Freiser (103) have compared the dipole moments of thiophene (0.53*D*), thianaphthene (0.62*D*), dibenzothiophene (0.83*D*), and tetrahydrothiophene (1.97*D*). These dipole moments are roughly parallel to the electron density around the sulfur and they indicate the decreasing availability of the unshared electrons of the sulfur in resonating systems. These investigators further ascribed the increase of dipole moments of thianaphthene and dibenzothiophene over thiophene to the increasing significance of resonance structures used to describe the ground states of these molecules which do not involve the unshared electrons of the sulfur atom. Several examples are shown below.





These dipole measurements agree qualitatively with experimental data which indicate that ease of sulfone formation is as follows:

sulfides > dibenzothiophene > thianaphthene > thiophene

The ease with which oxygen in furan systems coordinates with a positive ion should parallel the ease of sulfone formation in the thiophene systems.

CHAPTER II

Thianaphthene and Other Thiophene Compounds Containing One Carbocyclic Fused Ring

Introduction

This chapter summarizes the chemistry of condensed thiophene systems containing one carbocyclic ring, cyclopentathiophenes, thianaphthenes (benzothiophenes) and cycloheptathiophenes. Thianaphthene (benzo-[*b*]thiophene) is the best known compound of this series and makes up the bulk of the chapter. Isothianaphthene (benzo[*c*]thiophene) is known only in the form of derivatives. Cyclopenta- and cycloheptathiophenes are mere laboratory curiosities.

A. Thianaphthene and Its Derivatives

Although a large number of studies have been carried out on thianaphthene, there are still numerous problems to be solved. This is not the case with the hydroxythianaphthenes and quinones. Since these materials are the essential intermediates in the synthesis of commercial thioindigo dyes, they have been the subject of an intensive research program in several industrial laboratories and many academic institutions throughout the world. Almost every conceivable preparation and reaction of these materials has been reported.

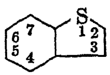
Komppa has carried out the only systematic study of the preparation of derivatives of thianaphthene. His work was of an exploratory nature and needs to be extended in many fields. For example, no attempt has been made to alkylate thianaphthene by means of the Friedel and Crafts reaction or by the recent methods for the alkylation of thiophene. Levine and coworkers have extended their own work and the work of Hartough and Kosak on the acylation of thiophene to the thianaphthene series. Many new studies of this nature should be undertaken. The current interest in antihistaminics warrants an investigation of the behavior of thianaphthene in the Mannich reaction. Halogenation of thianaphthene has only been studied in a superficial manner; a detailed study should prove exceptionally interesting.

Orientation studies in thianaphthene chemistry have been ignored by many of the investigators. True, it has been established that thianaphthene substitutes *predominantly in the 3-position,* but when careful studies had been carried out it was also established that a considerable amount of 2-substitution occurred. Failure of a majority of the investigators to recognize this fact has led to some rather doubtful chemistry. In addition to establishing the ratio of 2- to 3-isomers in normal substitution reactions, subsequent studies should be undertaken to establish the order and positions of substitution of the benzenoid ring of thianaphthene once the 2- and 3-positions have been substituted. Only one study (nitration) has thus far been reported on this subject.

Recently, thianaphthene was made available in semicommercial quantities by Jefferson Chemical Company. A brochure (547) describes the specifications of the available product and lists a short summary of some of the unpublished work carried out in the market development of this compound.

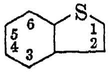
Nomenclature

Preferred Numbering and Nomenclature



(*Ring Index* No. 853)
Thianaphthene

Alternate Numbering and Nomenclature



The alternate numbering was used by English investigators for the period between 1906 and 1930. Alternate names for the system are benzo[*b*]thiophene, 1-thiaindene, thionaphthen, and benzothiofuran. *Chemical Abstracts* indexed this compound under thionaphthene from 1907–1936 but used the English numbering system for only a few years before converting to the German system now in use. The British abstracts still use the original British form, thionaphthen.

Occurrence of Thianaphthene in Nature

Although the original discovery of thiophene in coal tar by Victor Meyer in 1882 was a direct clue that condensed thiophene ring systems might also be present, it was not until 1902 that Boes (55) reported the isolation of thianaphthene from that source. He was able to separate thianaphthene from the naphthalene fraction of brown coal distillates by means of the picrate. He further stated thianaphthene was not present in peat tar or in "American crude oil."

Later, in 1918 and 1920, a process was patented for the removal of thianaphthene from the naphthalene fractions of coal tar by means of sulfuric acid (P-384,P-386). It was stated that a crude naphthalene fraction, which contained as much as 3% sulfur (12% thianaphthene), was extracted with sulfuric acid to yield an extract in which the thianaphthene content had been raised to 36%. Pure thianaphthene was separated in one case by means of reaction with mercuric acetate and subsequent regeneration from the thianaphthenemercuriacetate (P-384). In the other case (P-386), the pure thianaphthene was obtained from a 20–30% concentrate by first washing with alkali to remove phenols and then sulfonating the mixture with 66°Bé. sulfuric acid in carbon disulfide solution. Subsequent steam distillation of the sulfonic acid yielded pure thianaphthene.

Weissgerber and Kruber (522) studied processes for removing thianaphthene from crude coal tar naphthalene. They observe that sodium at high temperatures gave a vigorous reaction which resulted in the formation of sodium sulfide. This eventually led to a process of heating crude naphthalene with solid potassium hydroxide in an autoclave at 300° to lower the sulfur content of naphthalene (P-408). Weissgerber and Kruber (522) were not successful in the separation of appreciable amounts of pure thianaphthene by use of the concentrated sulfuric acid extraction process (P-384) and found that only 2 g. of pure thianaphthene could be obtained from 80 kg. of commerical naphthalene. Working with mixtures containing 12–14% sulfur they found that the use of mercuric acetate did not produce completely pure thianaphthene. A recent U.S. Patent (P-687) describes a process of concentrating thianaphthene from coal tar by crystallizing out a solid solution with naphthalene. The thianaphthene and naphthalene are then separated by an azeotropic distillation employing methylcarbitol.

Two methylthianaphthenes have been isolated from the methylnaphthalene fraction of coal tar (523). One of the isomers appears to be 2-methylthianaphthene, m.p. 52°. The other isomer described, m.p. 36°, may be the 5-methyl derivative, m.p. 36.5°, recently reported by Krollpfeiffer, *et al.* (574).

Weissgerber's broad studies on the distribution of sulfur compounds in coal tar led to the conclusion that these were almost exclusively built up of thiophene ring compounds (523). Maihle (367) showed the presence of ethyl and methyl mercaptans and sulfides in coal tar, but found thiophene and thianaphthene only in higher fractions. Thianaphthene has also been isolated from shale oil (98). A dimethylthianaphthene has been isolated from Karwendol oil (a high sulfur content Austrian shale oil possessing medicinal properties) (487).

From hydrodesulfurization experiments, Hoog (626) has predicted that the basic structures of the sulfur compounds in a Middle East gas oil consist of about 30–40% condensed thiophene systems which contain one homocyclic ring (thianaphthenes and hydrothianaphthenes) and 70–60% of condensed thiophene systems with two homocyclic rings (dibenzothiophenes and arylthianaphthene types).

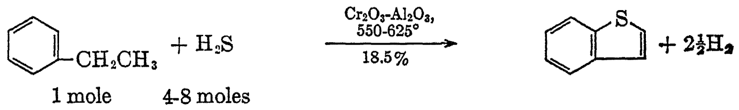
A method for determining small percentages of thianaphthene in the presence of naphthalene by means of infrared absorption spectra has been developed (665). The band at 9.48μ is selective for thianaphthene. Investigation of a commercial naphthalene sample showed 1.30% thianaphthene, agreeing very well with the figure of 1.26% calculated from the measured sulfur content of 0.30%. This also suggests that the bulk of the sulfur is present as thianaphthene.

I. Preparation of Thianaphthene and Its Homologs

Thianaphthene and its homologs are prepared by a variety of methods. The majority are based on closing the thiophene ring on the benzenoid ring. Starting materials include ethylbenzene or styrene, *o*-ethylthiophenol or *o*-vinylthiophenol, or a compound of the series, $C_6H_5SCH(R)$—COR', where R is H or alkyl and R′ is OH, OEt, alkyl, or aryl. Thianaphthene has been noted as a by-product in the synthesis of thiophene and thiophthene from acetylene and sulfur (386) or from acetylene and hydrogen sulfide (385), but these methods were not used extensively and probably involve the intermediate formation of styrene, which is subsequently ring closed by reaction with sulfur or hydrogen sulfide. A more difficult type of synthesis forms the benzene ring on the thiophene ring. Miscellaneous methods for the synthesis of homologs as well as aryl and heterocyclic derivatives are listed below.

A. Thianaphthene

Thianaphthene is available in semicommercial quantities from Jefferson Chemical Company, but the method of synthesis has not yet been revealed. It probably is made by some variation of the reaction of ethylbenzene or styrene with hydrogen sulfide or sulfur over a catalyst. (*Note:* A recent patent to Devaney (P-704), of the Texas Co. describes the reaction of styrene with sulfur at 1235°F. in the presence of a Cr_2O_3-SiO_2-Al_2O_3 catalyst This may be the process used.) This method as described by Hansch and Hawthorne (281) involves dehydrogenation of ethylbenzene and subsequent reaction of the styrene with hydrogen sulfide. This final

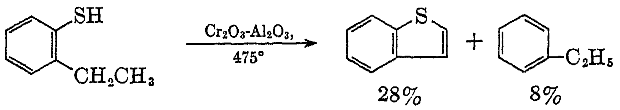


(1)

ring closure requires a second dehydrogenation step (eq. 1). The catalyst is 18.2% chromia on activated alumina. A nickel oxide-chromia-alumina gel-type catalyst may also be employed. It is preferable to reduce the catalyst with hydrogen at the reaction temperature, after which hydrogen sulfide is introduced for initial activation before charging the ethylbenzene.

Styrene may be employed in a similar process (391,P-604). In this reaction one mole of styrene and four moles of hydrogen sulfide are passed over alumina containing 5% iron oxides at 600°. When a 20-sec. contact time is employed, an ultimate yield of 60% of thianaphthene is obtained at a conversion of 23.4% per pass.

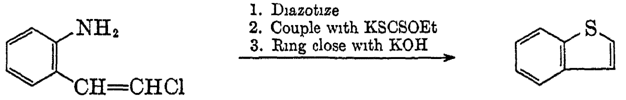
While the mechanism of the above reaction has not been clearly defined, Hansch and Blondon (280) have found that *o*-ethylthiophenol can be cyclized by a similar type of reaction (eq. 2).



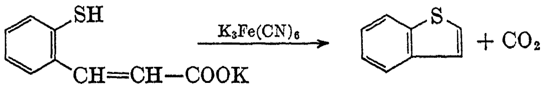
(2)

Thiophenol reacts with acetylene in the vapor phase at 600–650° to yield thianaphthene (71%) (745). *p*-Thiocresol yields 5-methylthianaphthene (54%) in the same manner.

The first and probably one of the most difficult syntheses of thianaphthene was accomplished by ring closure of 2-(2-chlorovinyl)aniline in the three-step synthesis (226) shown in Equation 3 below. Komppa (325a) had previously prepared benzofuran by this synthesis and subsequently prepared thianaphthene from the action of potassium hydroxide on 2-(2-chlorovinyl)thiophenol (326,327). A similar type ring closure can be accomplished in good yield from *o*-mercaptocinnamic acid (108) (eq. 4).

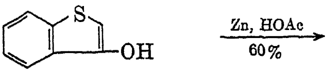


(3)



(4)

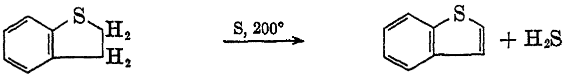
The most widely employed synthesis of thianaphthene and thianaphthene homologs is accomplished by reduction of 3-hydroxythianaphthenes (see section II below for complete synthesis) with zinc dust (46,14)



(5)

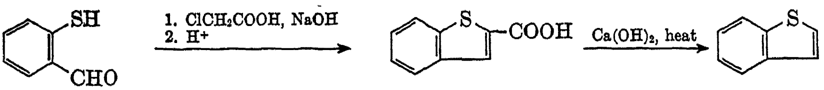
or by heating with zinc dust and acetic acid (371,278,279) (eq. 5). 3-Hydroxy-2-thianaphthenecarboxylic acid or its sodium salt may also be employed in this reaction (46).

Thianaphthene can be prepared from 2,3-dihydrothianaphthene by dehydrogenating with sulfur (67) (eq. 6). Hansch (279) reported that



(6)

thianaphthene obtained by reduction of 3-hydroxythianaphthene is contaminated with 2,3-dihydrothianaphthene and that pure thianaphthene is obtained by refluxing with 10% by weight of sulfur. This observation may account for the variety of melting points of some of the homologs of thianaphthene listed in Table II-3 because a majority of these were prepared by reduction of the 3-hydroxy derivatives.



(7)

Other types of synthesis involved decarboxylation of thianaphthenecarboxylic acids. Friedländer and Lenk (206) prepared thianaphthene from *o*-mercaptobenzaldehyde in a three-step synthesis (eq. 7).

B. Monoalkylthianaphthenes

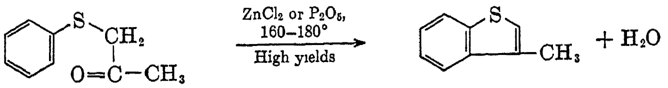
2-Methylthianaphthene is obtained in 43% yield from the reaction of 2-thianaphthenyllithium with methyl tosylate (736). It is also prepared by the method described in equation 2 from 2-*n*-propylthiophenol (280). Pure 3-methylthianaphthene cannot be isolated when this reaction is applied to 2-isopropylthiophenol. Werner (525) obtained 3-methylthianaphthene by dehydration of phenyl acetonyl sulfide (eq. 8). 3-Methylthianaphthene, as well as the 3-ethyl homolog, has been prepared

TABLE II-1. Physical Properties of Thianaphthene

Property		Ref.
B.p., °C. (mm.)	103–105 (20)	278
	220–221 (760)	327
	100 (16)	98
	221–222 (760)	22
	210–215 (760)	745
M.p., °C.	32	108, 279, 102, 386, 745
	30	327
	30–31	226
	31.2–31.4	P-604
	31–32	98
n_D^{39}	1.6306	547
n_D^{37}	1.63740	194
$n_D^{36.2}$	1.63324	22
$n_\alpha^{36.2}$	1.62509	22
$n_\beta^{36.2}$	1.65439	22
$n_\gamma^{36.2}$	1.67368	22
$d_4^{32.2}$	1.1484	22
Dipole moment $\mu \times 10^{18}$	0.62	103
Flash point, °C.	101.5	547
Kinematic viscosity centistokes		
at 54.5°C.	1.52	547
at 99.0°C.	0.85	547
Entropy (liquid at 304.50°K.)	53.31 cal. deg.$^{-1}$ mole^{-1}	744
Heat of fusion (304.50°K.)	2827 cal. mole^{-1}	744
Triple point	304.50°K.	744
Cryoscopic constant	0.01534 deg.$^{-1}$	744
Heat of transition (261.6°K.)	650.1 cal. mole^{-1}	744

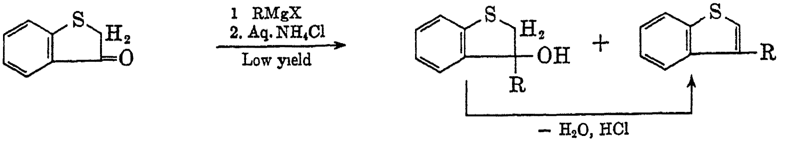
TABLE II-2. Thianaphthene Addition Complexes

Addition complex with	M.p., °C.	Reference
Picric acid	148–149	226, 98, 387, 745
	148.8–149	327, 386
Styphnic acid	136–137	98
2,4-Dinitrothiophene	Red-orange solid	471
2,5-Dinitrothiophene	41–43	471
1,3,5-Trinitrobenzene	148–150	90
Tetrachlorophthalic anhydride	Dissoc. >150°	750



(8)

by the action of a Grignard reagent on the oxo form of 3-hydroxythianaphthene (573,574) (eq. 9).



(9)

5-Methylthianaphthene was synthesized in 49% yield by reducing 5-methyl-3-hydroxythianaphthene with zinc dust and hydrochloric acid (504). 6-Methylthianaphthene has been prepared similarly (505).

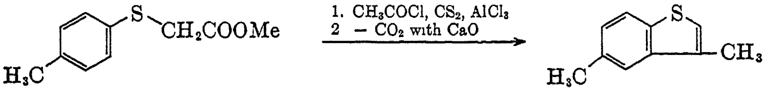
Preparation of monoalkylthianaphthenes by alkylation of thianaphthene is not reported, although this reaction probably could be accomplished by techniques recently established for thiophene. 3-Ethylthianaphthene, 3-*n*-propylthianaphthene, and 3-*n*-butylthianaphthene were obtained by Clemmensen reductions of the respective ketones in yields averaging about 60% of theory (77,82). The Wolff-Kishner reduction of ketones of this series is not reported.

The most recent, and apparently one of the most versatile syntheses, of thianaphthene has been announced by Tilak (761–768). The method involves addition of $C_6H_5SCH_2CH(OCH_3)_2$ to H_3PO_4-P_2O_5 at 170–180° under a vacuum of 10 mm. The resultant thianaphthene immediately distills from the reaction mixture in 72.5% yield. The method has been widely applied to phenyl-substituted R-$C_6H_4SCH_2CH(OCH_3)_2$ where R is halogen, methyl, or an alkoxy group yielding 5-, 6-, and 7-chlorothianaphthene, 7-bromothianaphthene, 5-, 6-, and 7-methylthianaphthene, and 5-, 6-, and 7-alkoxythianaphthenes. Yields vary from poor to 85% of theory. The method has also been applied to the synthesis of fused ring thianaphthenes (764–766) and to dibenzothiophene (768).

C. Dialkylthianaphthenes

2,3-Dimethylthianaphthene is prepared by the method illustrated in eq. 8 from 3-(phenylthio)-2-butanone in 85–95% yield (525).

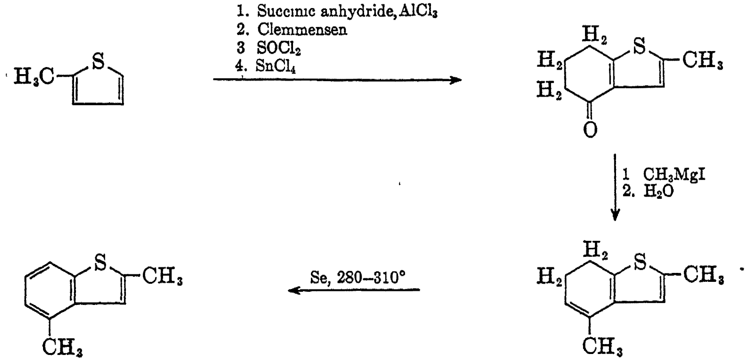
3,5-Dimethylthianaphthene is formed by the decarboxylation of the 2-carboxy derivative (P-474) eq. 10).



(10)

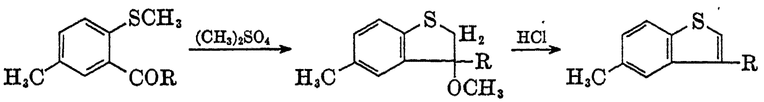
This method should be generally applicable to producing 3-alkyl derivatives when CH_3COCl in the above equation is replaced by RCOCl.

2,4-Dimethylthianaphthene has been prepared from 2-methylthiophene by the following reaction sequence (624) (eq. 11).



(11)

Krollpfeiffer and coworkers (573,574) have synthesized a number of thianaphthene homologs through a series of sulfonium salts. Their work indicates that this method should be widely applicable to a large variety of thianaphthene homologs. The original literature should be consulted for minute details of the mechanism. Generally, the reaction proceeds by the following sequences of reactions (eq. 12):



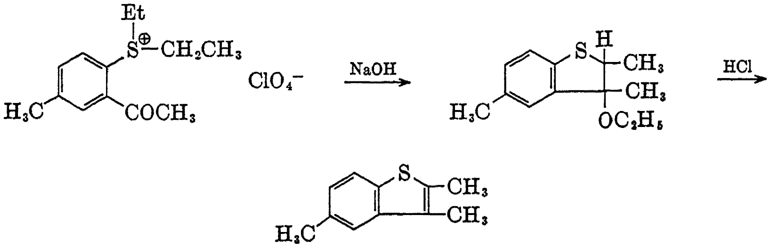
(12)

where R is CH_3, C_2H_5, iso-C_3H_7, and C_6H_5.

D. Trialkylthianaphthenes

2,3,5-Trimethyl- and 2,3,7-trimethylthianaphthene are obtained from the appropriate sulfide by the method described in equation 8 (525).

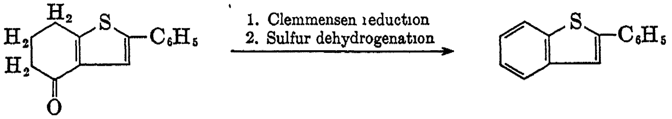
Krollpfeiffer and coworkers (573,574) have obtained 2,3,5-trimethylthianaphthene through a condensation of the following sulfonium salt (eq. 13).



(13)

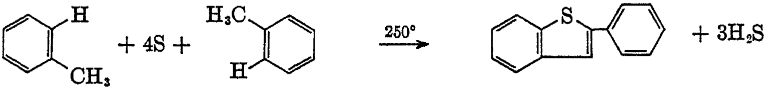
E. Arylthianaphthenes

2-Phenylthianaphthene has been synthesized by a modification of the usual synthesis of 4-hydroxythianaphthene (184,318). Horton (300) has treated 2-phenylthiophene with succinyl chloride and reduced the corresponding ketone to 2-phenyl-5-thienylbutyric acid. This acid was subsequently cyclized to 2-phenyl-4,5,6,7-tetrahydrothianaphthene-4-one which was converted to 2-phenylthianaphthene as shown in eq. 14. This synthesis should be generally applicable to the preparation of 2-substituted thianaphthenes, but it has been applied in only one case (with still another modification) to the synthesis of 2,4-dimethylthianaphthene (see eq. 11).



(14)

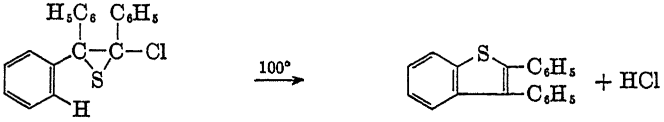
2-Phenylthianaphthene has also been shown to be formed along with 2,3,4,5-tetraphenylthiophene (thionessal) when toluene was heated with sulfur at 250° (eq. 15). Horton postulates a free radical mechanism for this dehydrogenation and cyclization. The same mechanism applies to the reaction of sulfur and diphenyl sulfide at 200°, to the heating of diphenyl disulfide, and to the action of sulfur on barium phenyl acetate, all of which yield the same end product.



(15)

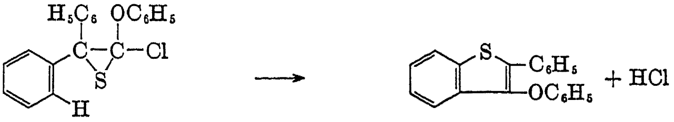
5-Methyl-3-phenylthianaphthene has been prepared by the method outlined above (eq. 12) by treating 2-benzoyl-4-methylthioanisole with methyl sulfate and hydrogen chloride (573,574).

2,3-Diphenylthianaphthene has been prepared in the manner described in eq. 16; however, the structure has not been substantiated fully



(16)

(464). Schönberg and Vargha (444) demonstrated that 1,1-diphenyl-2-phenoxy-2-chloroethylene sulfide prepared from diphenylacetonitrile and C_6H_5OCSCl, rearranged to 2-phenoxy-3-phenylthianaphthene (eq. 17).

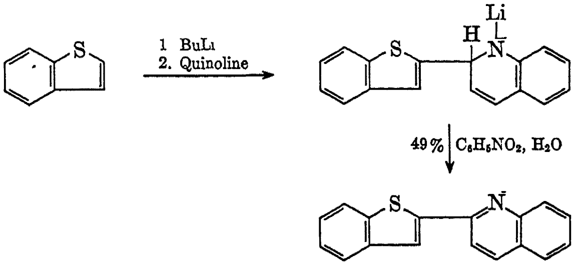


(17)

These same investigators prepared the 2-thiophenyl derivative and 2-phenoxy-3-*p*-tolyl-6-methylthianaphthene by the same method, the latter being prepared from 1,1-di-*p*-tolyl-2-phenoxy-2-chloroethylene sulfide.

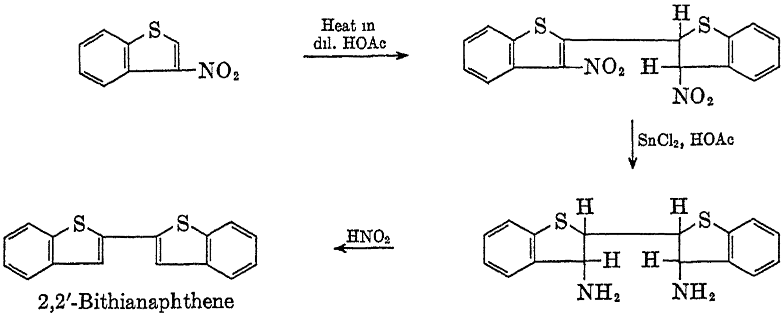
Other aryl derivatives reported in the literature are 3-quinolinyl (76,80) and 3-indolyl (86) derivatives. These are prepared from 3-thianaphthenyl ketones. Their syntheses are discussed in section VIII. Their physical constants are listed in Table II-3.

2-(2′-Quinolinyl)thianaphthene is formed from the addition of 2-thianaphthenyllithium to quinoline followed by oxidation of the intermediate with nitrobenzene and water (605) (eq. 18).

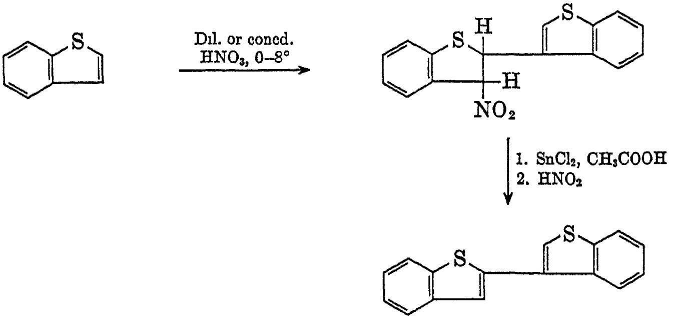


(18)

2,2′-Bithianaphthene and 2,3′-bithianaphthene are reported to be formed through polymerization reactions of 3-nitrothianaphthene. Fries and Hemmecke (220) indicate that the reactions take place by the following sequence of reactions (eqs. 19 and 20). The mechanism appears to be



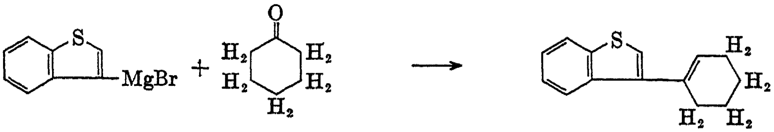
(19)



(20)

quite similar to that described for the polymerization of thiophene (603). 2,2′-Bithianaphthene also results from the coupling action of bromine on 2-thianaphthenyllithium (736).

3-(1-Cyclohexenyl)thianaphthene has been prepared by condensation of cyclohexanone and 3-thianaphthenylmagnesium bromide (537) (eq. 21).

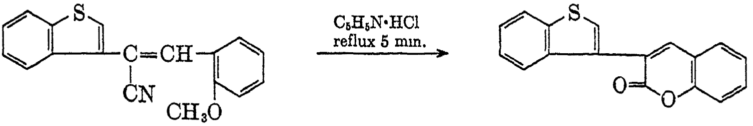


(21)

3-(3′,4′-Dihydro-1′-naphthyl)thianaphthene was synthesized in the same manner from α-tetralone and was dehydrogenated to give 3-(1′-naphthyl)-thianaphthene by heating with sulfur at 220–240° (537).

Vinylthianaphthenes are not reported in the literature. Only two ethylene derivatives have been synthesized. 1-Phenyl-2-(3′-thianaphthenyl)ethylene is formed when 3-thianaphthenecarboxaldehyde is treated with benzylmagnesium chloride (676). 1-(2′,4′,6′-Trinitrophenyl)-2-(3′-thianaphthenyl)ethylene is obtained in quantitative yield by refluxing the 3-aldehyde with TNT (676).

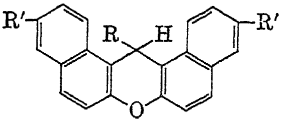
The formation of 3-(3′-coumarinyl)thianaphthene is illustrated by



(22)

reaction 22 (676). Replacement of the *o*-anisyl radical of I with the 2-methoxy-1-naphthyl radical yields the corresponding 5,6-benzo derivative of II.

When 2-naphthols are refluxed with 3-thianaphthenecarboxaldehyde in acetic acid and a trace of hydrogen chloride, dibenzoxanthene derivatives of structure III result (676).



R′ = H, R = 3-thianaphthenyl, m.p. 280° R′ = Br, R = 3-thianaphthenyl, m.p. 235

II. Miscellaneous Reactions and Properties

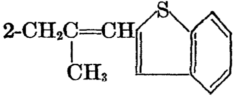
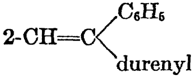
In general, the reactions of thianaphthene are discussed under the sepa rate categories devoted to the functional groups. Only a few specifi reactions are discussed in this subdivision.

As might be anticipated, the chemical reactions of thianaphthene hav not been as thoroughly investigated as those of thiophene. Only cursory investigations of halogenation have been undertaken and major reactions such as alkylation are not reported at all. Komppa has made the only systematic investigation of the reactions of thianaphthene. Levine at the University of Pittsburgh and Bordwell at Northwestern University have recently begun a series of studies to determine isomer formation in thianaphthene substitution, but only the early results of these investigations can be included in this report. The early indications from acylation studies indicate that both the 2- and 3-isomers form in substitution reactions. In view of the high percentage of the 2-isomer reported, the authenticity of the older work, which reported only 3-substitution products, should be questioned until some of this work is reinvestigated.

Thianaphthene can be stored in amber bottles or tin cans (547). Continued exposure to light and the atmosphere results in the formation of a

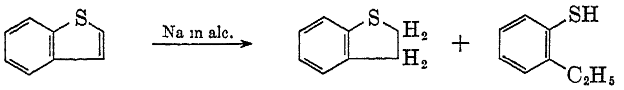
TABLE II-3. Physical Properties of Thianaphthene Homologs and Aryl Derivatives

Substituent	B.p., °C. (mm.)	M.p., °C.	n_D^t	d_4^t	M.p. °C. of picrate	Ref.
2-Methyl	—	51–52	$n_\alpha^{99.7}$ 1 57608	1.0490 (99.7)	108–109	523,24,280, 736
			$n_\beta^{99.7}$ 1 60204	—	—	523
3-Methyl	125–127 (25)	—	1.6229 (20)	1 1190 (20)	119–120	525,573
	108–109 (12)	—	1.6268 (20)	1 137 (20)	122 5–123.5	759
5-Methyl	105–110 (13)	20–22	—	—	—	504,745
	111–115 (12)	19–22	1.6155 (20)	1.113 (20)	—	22
		36 5	—	—	110.5–111	574,745,762
			n_α 1 60730 n_D 1 61476 n_β 1 68374 n_γ 1 65141 (21 65°)	—	—	22
6-Methyl	110–115 (3)	42–42 5	—	—	114–115	505,762,767
7- or 4-Methyl	—	36	—	—	—	523
7-Methyl	110–115 (4)	—	—	—	144–145	762
2,3-Dimethyl	122–124 (13)	—	1.6170 (20)	1 1054 (20)	101–102	525
2,4-Dimethyl	132–135 (15)	—	—	—	100–101	624
3,5-Dimethyl	119 5–120 (9)	—	—	—	113–114	573,574, P-474
3-Ethyl	180 (83)	—	—	—	78	77
3-Ethyl-5-methyl	145 (17)	—	—	—	87–88	574
2,3,5-Trimethyl	144–146 (13)	56–57	1.6022 (20)	—	124 5–125 5	525
					125–126	573
2,3,7-Trimethyl	143–144 (13)	51–52	1.6080 (20)	—	110–110 5	525
3-*n*-Propyl	174–176 (24)	—	—	—	—	82
3-*n*-Butyl	184–186 (24)	—	—	—	—	82
3′-CH_2-3′-thianaphthenyl	280–282 (13)	—	—	—	—	676
2-Phenyl	—	177.5–176 0	—	—	—	300
3-Phenyl-5-methyl	162 (1)	—	—	—	Does not form	300

Substituent	B.p., °C. (mm.)	M.p., °C.	n_D^t	d_4^t	M.p. (°C.) of picrate	Ref.
2,3-Diphenyl	—	114	—	—	—	464
3-(1′-Naphthyl)	165 (1)	Oil	—	—	—	537
2-(2′-Thianaphthenyl)	—	262	—	—	—	220,736
2-(3′-Thianaphthenyl)	—	76	—	—	—	220
2-(2′-Quinolinyl)	—	189 8–189.9	—	—	221.5–222	605
3-(9′-Xanthenyl)	—	172–173	—	—	—	6
3-(3′-Coumarinyl)	—	181	—	—	—	676
3-(6′-Bromo-3′-coumarinyl)	—	223	—	—	—	676
3-(5′,6′-Benzo-3′-coumarinyl)	—	222	—	—	—	676
3-(2′-Quinolinyl)	—	186	—	—	—	76
3-(3′-Methyl-2′-quinolinyl)	—	76	—	—	234–235	80
3-(3′-Ethyl-2′-quinolinyl)	—	98	—	—	175–176	80
3-(3′-*n*-Amyl-2′-indolyl)	293–295 (13)	—	—	—	—	86
3-(3′-*n*-Hexyl-2′-indolyl)	280–285 (10)	—	—	—	—	86
3-(3′-*n*-Heptyl-2′-indolyl)	286–288 (10)	—	—	—	—	86
3-(3′-*n*-Octyl-2′-indolyl)	290–294 (10)	—	—	—	—	86
3-(3′-*n*-Nonyl-2′-indolyl)	295–298 (10)	—	—	—	—	86
3-(3′-*n*-Decyl-2′-indolyl)	300–302 (10)	—	—	—	—	86
3-(3′-*n*-Dodecyl-2′-indolyl)	310–312 (10)	—	—	—	—	86
3-(3′-*n*-Tetradecyl-2′-indolyl)	320–322 (11)	—	—	—	—	86
3-(1′-Cyclohexenyl)	135 (0.1)	—	—	—	—	537
3-(3′,4′-dihydro-1′-naphthyl)-	Oil	—	—	—	—	537
3-CH=CH-C_6H_5	238–242 (13)	—	—	—	—	676
3-CH=CH-(2′,4′,6′-tri NO_2-C_6H_2)	—	182	—	—	—	676
	—	111 6–113 and 121–122	—	—	—	737
 $2\text{-CH}{=}\text{C}(\text{C}_6\text{H}_5)(\text{durenyl})$	—	163.8–164 6	—	—	—	737

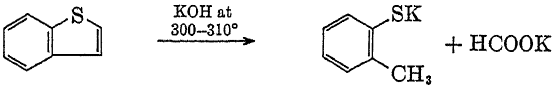
in the presence of hydrogen fluoride (319). Milder catalysts causing polymerization of thiophene, such as sulfuric acid, phosphoric acid, and activated clays, have not been investigated. Thianaphthene copolymerizes to form a simple dimer with 3-nitrothianaphthene during nitration with dilute or concentrated nitric acid at 0–8° (220) (see section I, eq. 21). In a somewhat similar manner, 3-nitrothianaphthene dimerizes when heated in dilute acetic acid (220) (see section I, eq. 20).

Chemical hydrogenation of thianaphthene gives 2,3-dihydrothianaphthene and *o*-ethylthiophenol (192,193) (eq. 23). Since the sulfur atom of thianaphthene caused the usual "sulfur-poisoning" of most hydrogenation catalysts, the hydrogenation of thianaphthene over such catalysts has not been accomplished. Detoxification of naphthalene containing thianaphthene toward platinum catalysts has been accomplished by a two-step process which absorbs the trace amounts of thianaphthene on the catalyst surface where it is oxidized to the 1-dioxide. In this form, the sulfur is nontoxic to the catalysts (376,377). Mild hydrogenation of thianaphthene with sulfur-resistant catalysts is not reported.



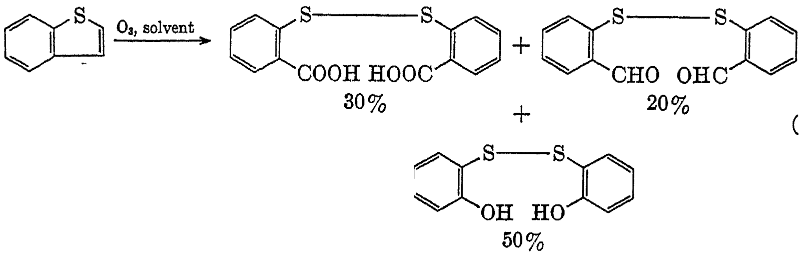
(23)

Rupture of the thiophene ring of thianaphthene has been accomplished by several means. Sodium in alcohol gives *o*-ethylthiophenol (192,193). Fusion of thianaphthene with potassium hydroxide gives a low yield of *o*-methylthiophenol (524) (eq. 24).



(24)

While hydrogen peroxide converts thianaphthene to the 1-dioxide, the more vigorous action of ozone causes ring rupture, producing a variety of products (514) (eq. 25). Raney nickel alloy removes sulfur from



(25)

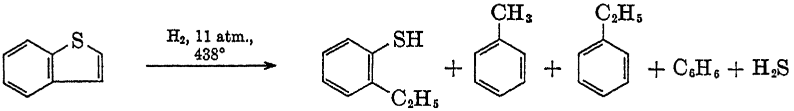
thianaphthene and its derivatives (51a,53,403,627). This method should prove useful in the future for structure studies. Table II-4 lists the compounds reduced and the respective products obtained.

TABLE II-4. Raney-Nickel Reduction of Thianaphthene Compounds

Compounds reduced	Products	Yield, %
Thianaphthene	Ethylbenzene	75
3-Hydroxythianaphthene	Ethylbenzene	86
2-Thianaphthenecarboxylic acid	$C_6H_5CH_2CH_2COOH$	93 4
3-Thianaphthenecarboxylic acid	$C_6H_5CH(CH_3)COOH$	93, 98
Diphenyl-3-thianaphthenylacetic acid	$C_6H_5CH(CH_3)C(C_6H_5)_2COOH$	82 5
4-Hydroxythianaphthene	*o*-Ethylphenol and *o*-ethylthiophenol	48 and 42
2,3-Thianaphthenequinone	Mandelic acid	
5-Methyl-2,3-thianaphthenequinone	*m*-Methylmandelic acid	
Thioindigo (durindone Red B)	Diphenacyl 1,4-Diphenylbutane Benzoic acid	Low
5,5′-Diethoxythioindigo (durindone Orange R)	4,4′-Diethoxydiphenacyl *p*-Ethoxybenzoic acid	79

Attempts to fluorinate thianaphthene with cobalt trifluoride at 330–390° caused complete degradation of the heterocyclic ring and the only products that could be isolated were perfluorocyclohexane and perfluoroethylcyclohexane (742).

The thiophene ring of the thianaphthene nucleus is almost quantitatively ruptured in the presence of hydrogen without aid of a catalyst (193) (eq. 26). The reaction also produced some anthracene, as well as methane and ethane. Only a trace of 2,3-dihydrothianaphthene was detected.



(26)

Thianaphthene is said to be removed from naphthalene by use of 3–15% acid clay at 200° or activated acid clay at 150° (P-674).

Only a few color reactions of thianaphthene have been studied. Isatin produces the usual blue color of the indophenine test with 4-hydroxythianaphthene (49). Ceric nitrate alcohol reagent produces a brown color similar to thiophene and dibenzothiophene (652). Color reactions of several thianaphthene homologs with sulfuric acid have been reported (573,574).

Neither the toxicity nor the physiological activity of thianaphthene has been investigated fully. Preliminary data appear to indicate it to be less toxic to animals than benzene (547). From the published data up to the end of 1951 there seems to be no indication that introduction of thianaphthene into a specific drug in the place of a homocyclic ring system will impart any startling new properties to the drug. In most respects, it is indicated that the thianaphthene molecule retards the activity, particularly in antihistamine and plant hormone type compounds.

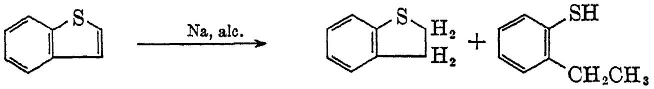
One report (644) indicates that both naphthalene and thianaphthene have good antimycotic activity for the larvae of *Coniphora cerebella*, *Poria vaporaria*, and *Lentinus lepideus*. Toxicity of thianaphthene toward the eggs and larvae of *Hylotrupes bajulus* has been clearly manifested. Thianaphthene was also shown to be very toxic to the larvae of the powder-post beetle (*Anobium punctatum*).

III. The Hydrothianaphthenes

This class of compounds is not well known and only a limited study of their reactions and derivatives has been undertaken. The methods used in their syntheses are almost as varied as the types of derivatives listed in Table II-5 of physical constants.

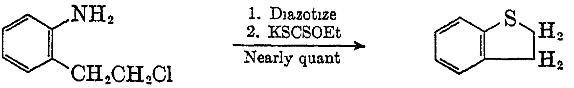
A. 2,3-Dihydrothianaphthene and Its Derivatives

The first synthesis of this compound involved a chemical reduction of thianaphthene with sodium in alcohol (193). In addition to 2,3-dihydrothianaphthene, a considerable amount of *o*-ethylthiophenol was formed by ring rupture of the dihydrothiophene ring (eq. 27). The thiophene ring of thianaphthene or 2,3-dihydrothianaphthene is very easily ruptured and no satisfactory catalytic or noncatalytic hydrogenation has been developed. Fricke and Spilker (193) indicated that in the absence of a hydrogenation catalyst, only trace amounts of 2,3-dihydrothianaphthene could be formed by the action of hydrogen on thianaphthene under 111 atm. pressure at 438°. No thianaphthene was recovered. The principal products were *o*-ethylthiophenol, hydrogen sulfide, toluene, ethylbenzene, benzene, and methane and its homologs.



(27)

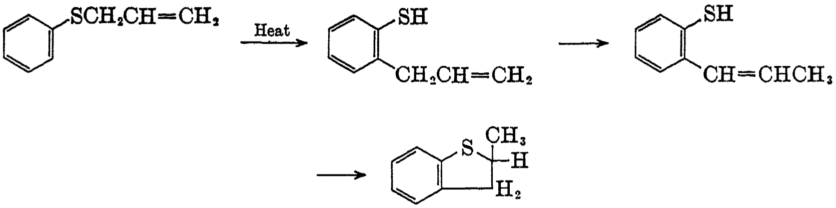
Bennett and Hafez (43) prepared 2,3-dihydrothianaphthene by the classical synthesis first used for thianaphthene. *o*-(2-Chloroethyl)-aniline, when diazotized and treated with potassium xanthate, cyclizes to form the desired compound (eq. 28).



(28)

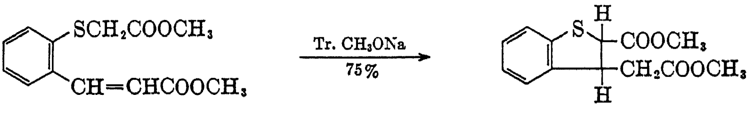
Bordwell and McKellin (722) obtained 2,3-dihydrothianaphthene 1-dioxide from thianaphthene 1-dioxide in high yields when palladium and hydrogen were employed. Lithium aluminum hydride reduced the latter compound to 2,3-dihydrothianaphthene in 92% yield.

2-Methyl-2,3-dihydrothianaphthene is formed by heating phenyl allyl sulfide (303). It appears that the following series of rearrangement reactions are involved (eq. 29).



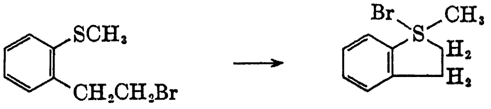
(29)

Koelsch and Stevens (620) suggested that the product formed by treating methyl *o*-mercaptocinnamate *S*-acetate with sodium methoxide was the dimethyl ester of 2-carboxy-2,3-dihydrothianaphthene-3-acetic acid (eq. 30). The free acid was formed by the usual saponification with alkali hydroxides. In addition, a second compound, $C_{11}H_8O_3S$, perhaps the anhydride of the acid, formed when the mixture was acidulated.



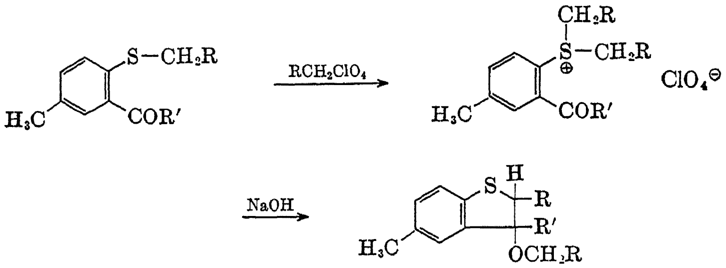
(30)

Bennett and Hafez (44) proposed that certain reactions of *o*-(2-bromoethyl)phenyl methyl sulfide indicated that the compound existed in the form of a sulfonium salt (eq. 31). This compound formed a crystalline chloroplatinate (see Table II-5).



(31)

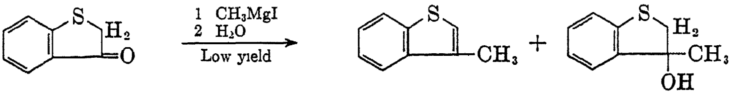
Krollpfeiffer and coworkers (573) have isolated a series of 2,3-dihydrothianaphthenes from the action of caustic on certain sulfonium salts. While the original article should be consulted for details, eq. 32 demonstrates a typical reaction. In the above equation, R is H or CH_3 and R′ is CH_3,



(32)

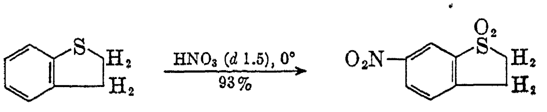
C_2H_5, iso-C_3H_7, or phenyl. Subsequent treatment with dimethyl sulfate causes removal of RCH_2OH to produce the fully aromatic thianaphthene derivative.

An intermediate 3-hydroxy-3-methyl-2,3-dihydrothianaphthene is formed along with 3-methylthianaphthene when 3-hydroxythianaphthene (*keto*-form) is treated with methylmagnesium chloride (573) (eq. 33).



(33)

2,3-Dihydrothianaphthene adds methyl iodide slowly to form a methiodide (67). It is converted to the 1-dioxide (sulfone) by oxidation (193,67). It forms a mercuric chloride complex readily (193) and reacts with aqueous mercuric acetate (714). Nitric acid converts 2,3-dihydrothianaphthene to 6-nitro-2,3-dihydrothianaphthene 1-dioxide (100) (eq. 34). The same compound results from the nitration of 2,3-dihydrothianaphthene 1-dioxide.

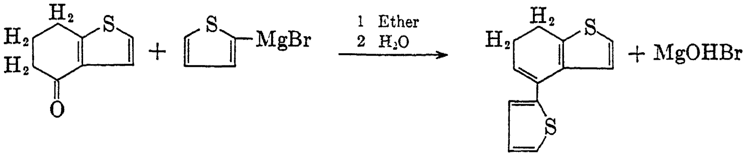


(34)

The sulfones of 2,3-dihydrothianaphthene are discussed in more detail in section XIV below. The physical constants of this series are listed in Table II-24 of that section.

B. 6,7-Dihydrothianaphthene

The parent compound of this series is unknown, but 4-(2-thienyl)-6,7-dihydrothianaphthene has been synthesized by reacting 2-thienylmag-



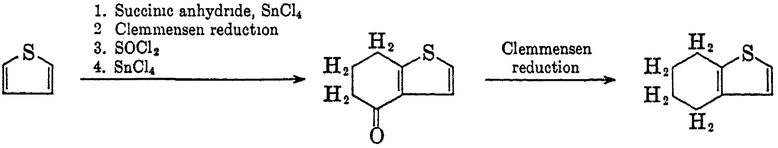
(35)

nesium bromide with 4-oxo-4,5,6,7-tetrahydrothianaphthene (537) (eq. 35). The reaction proceeds through the tertiary alcohol derivative which spontaneously dehydrates to produce the unsaturated derivative shown in the equation. 2,4-Dimethyl-6,7-dihydrothianaphthene has been synthesized in a similar manner but in this instance a dimer is also formed (624).

C. 4,5,6,7-Tetrahydrothianaphthene and Its Derivatives

4,5,6,7-Tetrahydrothianaphthene is prepared by a series of reactions starting with thiophene. The intermediate 4-oxo-4,5,6,7-tetrahydrothianaphthene (184,79) is conveniently reduced to the desired compound by means of the Clemmensen reaction (535).

The 2-methyl (624), 2-ethyl (615), 2-phenyl (300), and 2-chloro (625) derivatives of I are prepared by employing the appropriately substituted thiophene in the original reaction (eq. 36). Kitchen and Sandin (318)

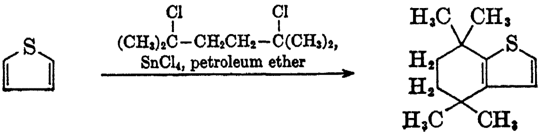


(I) (II)

(36)

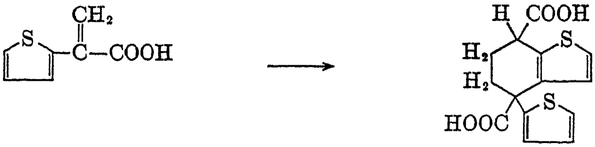
have prepared 4-oxo-5-methyl-4,5,6,7-tetrahydrothianaphthene from thiophene and methylsuccinic anhydride by this method, but did not reduce the ketone to the parent tetrahydrothianaphthene. This was also true of the 6-methyl derivative, which was prepared by a closely related method (705).

Another compound of this class, 4,4,7,7-tetramethyl-4,5,6,7-tetrahydrothianaphthene, is reported to form from the alkylation of thiophene with 2,5-dichloro-2,5-dimethylhexane (70) (eq. 37). The yield was not reported nor was the structure established.


$(CH_3)_2CCl-CH_2CH_2-CCl(CH_3)_2$,
$SnCl_4$, petroleum ether

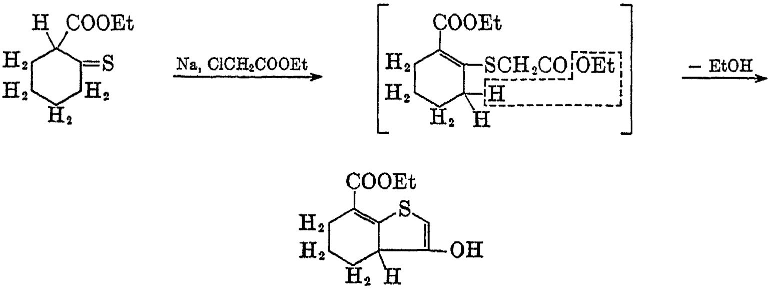
(37)

The dimer of 2-(2′-thienyl)acrylic acid is reported by Steinkopf and Wolfrom (470) to be a derivative of 4,5,6,7-tetrahydrothianaphthene and assigned the structure of 4-(2′-thienyl)-4,5,6,7-tetrahydrothianaphthene-4,7-dicarboxylic acid (eq. 38). Again, the structure was not established in an absolute manner.



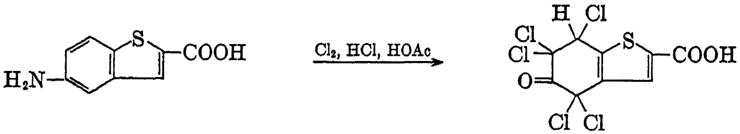
(38)

Another compound of doubtful structure, 3-hydroxy-7-carbethoxy-3a,4,5,6,-tetrahydrothianaphthene, is said to be formed from ethyl 1-thiocyclohexan-1-one-2-carboxylate and ethyl chloroacetate in the presence of sodium (101); the reaction probably takes place as shown in eq. 39.



(39)

5-Oxo-4,4,6,6,7-pentachloro-4,5,6,7-tetrahydro-2-thianaphthenecarboxylic acid has been prepared by the chlorination of 5-amino-2-thianaphthenecarboxylic acid in the presence of hydrogen chloride (222) (eq. 40). This compound decomposes at its melting point, 172°, and loses



(40)

one mole of hydrogen chloride and yields 5-oxo-4,4,6,7-tetrachloro-4,5-dihydro-2-thianaphthenecarboxylic acid.

4,5,6,7-Tetrahydrothianaphthene yields 2-substituted ketones when reacted with acyl chlorides in the presence of aluminum chloride (535). The 2-mercurichloride derivative is formed by standard methods (535). These derivatives are tabulated in Table II-5.

TABLE II-5. The Hydrothianaphthenes and Their Derivatives

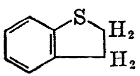
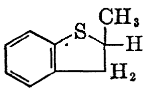
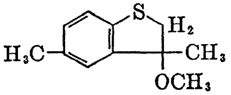
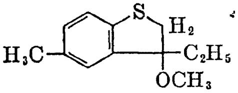
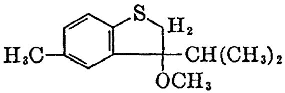
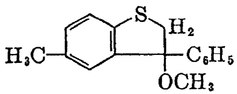
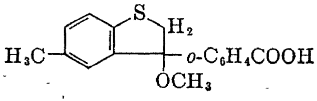
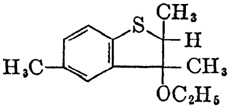
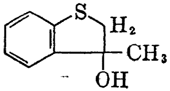
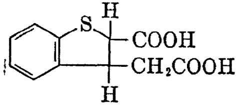
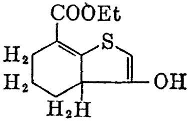
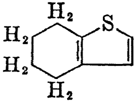
Compound	Ref.	B.p., °C. (mm.)	d_4^t	n_D^t	Deriv.	M.p., °C.	Ref.
	193	233.3–234 5 (768)	1.1125 (20)		$HgCl_2$ complex	128–129	193
	194	—	1 1036 (37)	1.63740 (37)	CH_3I	—	67
	67	104 (13)	1 129 (21)		CH_3Br-chloroplatinate	100 (dec.)	44
	43	105–107 (13 5)	—		—	—	
	100	110–111 (18)	—		—	—	
	303	103–108 (8)	—	1.5811 (20)	—	—	
	573	154–155.5 (16) M.p. 42–43	—	—	—	—	
	573	143–145 (10)	—	—	—	—	
	573	157–158 (12)					
	573	M.p. 150.5–151 5					

Table continued

TABLE II-5 (*continued*)

Compound	Ref.	B.p., °C. (mm.)	d_4^t	n_D^t	Deriv.	M.p., °C.	Ref
	574	M.p. 148–151					
	573	143.5–144 (8)					
	573	M.p. 58–59					
	620	143–144	—	—	Dimethyl ester Anhydride	B.p. 160–162 (4) 238–240	620 620
	101	M.p. 59					
	535	97 (19)	1.090 (20)	1.5572 (20)	2-HgCl	228	535

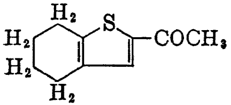
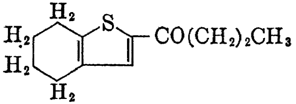
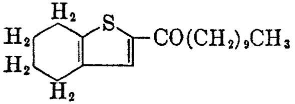
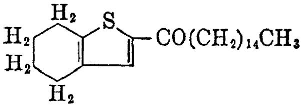
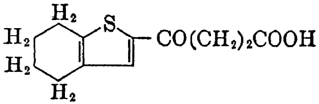
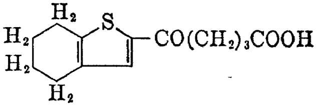
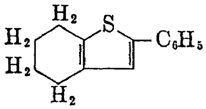
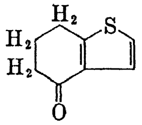
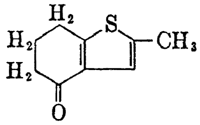
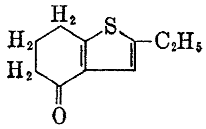
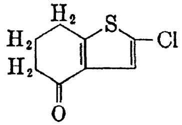
Compound	Ref.	B.p., °C. (mm.)	d_4^t	n_D^t	Deriv.	M.p., °C.	Ref.
	535	189 (22)	—	—	Semicarbazone	275	535
	535	199–200 (23)	—	—	Semicarbazone	245	535
	535	258 (18.5)	—	—	Semicarbazone	156	535
	535	300 (19)	—	—	Semicarbazone	119	535
	535	226 (16) M.p. 60	—	—	Methyl ester	73 B.p. 232 (15 mm.)	535
	535	M.p. 113	—	—	Ethyl ester	50 B.p. 245 (13 mm.)	535

Table continued

TABLE II-5 (*continued*)

Compound	Ref.	B.p., °C. (mm.)	d_4^t	n_D^t	Deriv.	M.p., °C.	Ref
	300	M.p. 82.5–83.5					
	184,79	102–110 (2) M.p. 35.5–37					
	624	149–150 (14) M.p. 29–30					
	615	161 (16)	—	—	Semicarbazone	219	615
	625	170 (20)	—	—	Semicarbazone	219	625

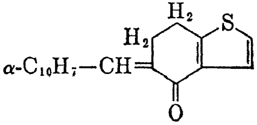
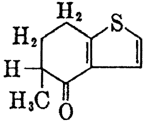
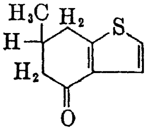
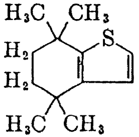
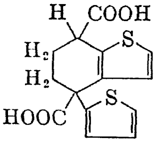
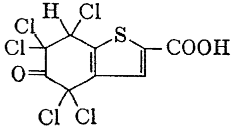
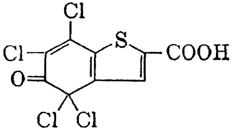
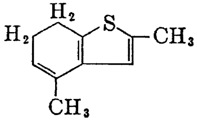
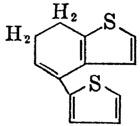
Compound	Ref.	B.p., °C. (mm.)	d_4^t	n_D^t	Deriv.	M.p., °C.	Ref.
	637	M.p. 118	—	—	Picrate	108	637
	318	Liquid					
	705	141–141 5 (10 7) M.p. 69	—	—	Oxime Semicarbazone 2,4-Dinitrophenylhydrazone Azomethine	149–149.5 188–189 259 5 249	705 705 705 705
	70	94 (6)					

Table continued

TABLE II-5 (*continued*)

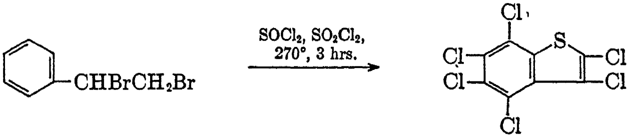
Compound	Ref.	B.p., °C. (mm.)	d_4^t	n_D^t	Deriv.	M.p., °C.	Ref.
	470	M.p. 216					
	222	M.p. 172					
	222	M.p. 213 (dec.)					
	624	128–132 (20)	—	—	Dimer	B.p. 270–275 (20)	624
	537	127 (0.05) M.p. 32–33					

4-Oxo-4,5,6,7-tetrahydrothianaphthene condenses with aromatic aldehydes at the 5-position much in the same manner as α-tetralone. Thus, when reacted with 1-naphthaldehyde in the presence of alcoholic hydroxide, the 5-(1′-naphthylidenyl)-4-oxo-6,7-dihydrothianaphthene is formed (637). The activity of the acyl group is further demonstrated in Chapter VIII, where details of ring closures involving the Fischer indole synthesis and the Pfitzinger reaction are found.

IV. Halogen Derivatives

There has been no systematic study of the halogenation of thianaphthene. Komppa (328) was the first to chlorinate thianaphthene. He reported that chlorine and thianaphthene gave a dichlorothianaphthene. Presumably this product was 2,3-dichlorothianaphthene, but no structure proof was undertaken. Later investigators (724) were able to prepare 3-chlorothianaphthene in 32% yield by treating thianaphthene with chlorine in carbon tetrachloride solution. These investigators also obtained Komppa's 2,3-dichlorothianaphthene in 83.5% yield. Chlorination of thianaphthene with iron as a catalyst yielded 13% of a mixture of tetrachlorothianaphthenes and a pentachlorothianaphthene. 6-Chloro-4-methylthianaphthene has been prepared by the reduction of 6-chloro-4-methyl-3-hydroxythianaphthene with zinc dust and hydrochloric acid (378,P-417).

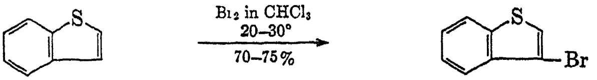
2,3,4,5,6,7-Hexachlorothianaphthene has been synthesized as shown in eq. 41 (32). Ring closures of various substituted phenyl methyl carbinols with thionyl chloride (32) are reported in their respective sections below (sections VI-B-6 and VI-B-7-e).



m.p. 158°

(41)

Bromination of thianaphthene yields a variety of products. Gattermann and Lockhardt (226) first reported that bromine water and thianaphthene gave a crystalline bromo derivative. Later, Komppa (327) reported that bromination yielded a dibromo derivative which upon further bromination gave a tribromo derivative. A tetrabromo derivative has also been reported (385). 3-Bromothianaphthene has been prepared by several investigators (328,78,P-598,52,518, 537). A normal procedure is described below (eq. 42). Bromination with *N*-bromosuccinimide also



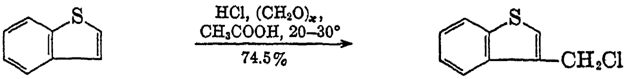
(42)

yields 3-bromothianaphthene (78). 2-Bromothianaphthene results from the treatment of 2-thianaphthenyllithium with bromine in ether solution (736).

Only three iodo derivatives of thianaphthene are reported. Iodination of thianaphthene in the presence of mercuric oxide yields a monoiodothianaphthene (presumably the 3-isomer) (327,P-707,776). 2-Iodothianaphthene results from treatment of 2-thianaphthenyllithium with iodine in ether (776). 2,3-Diiodothianaphthene has been prepared by treating 2,3-thianaphthenedimercurichloride with iodine in carbon tetrachloride (748).

Mixed halothianaphthenes have been prepared by treating 3-chloro-2-thianaphthenemercurichloride with either bromine or iodine in carbon tetrachloride. 3-Chloro-2-bromothianaphthene and 3-chloro-2-iodothianaphthene result. The former compound also results from direct bromination of 3-chlorothianaphthene in acetic acid solution (748).

Thianaphthene can be chloromethylated to give 3-chloromethylthianaphthene (51a,27,90,533,P-706) (eq. 43). Recent investigators (676)



(43)

b.p. 124–126° (2 mm.)
m.p. 44–45°

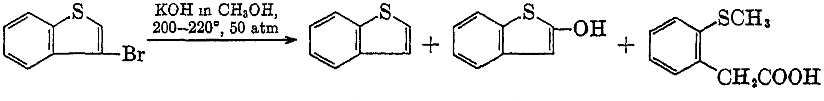
have reported that di-(3-thianaphthenyl)methane also is formed in this reaction. 2-Bromo-3-bromomethylthianaphthene can be prepared by bromination of 2-bromo-3-methylthianaphthene with *N*-bromosuccinimide (776).

3-Thiocyanatomethylthianaphthene results from the reaction of 3-chloromethylthianaphthene and potassium thiocyanate (724).

2-Chloromethylthianaphthene has been prepared in 79% yield by the action of thionyl chloride on 2-thianaphthenecarbinol (52). 2-(3-Thianaphthenyl)ethyl bromide has been obtained by treating the corresponding alcohol with phosphorus tribromide in pyridine solution (90).

Halogenations of derivatives of thianaphthene containing functional groups such as amino, nitro, carboxy, etc. are discussed under these respective categories.

Only a few of the possible reactions of 3-bromothianaphthene are reported. It can be converted to 3-thianaphthenecarboxylic acid through a typical Grignard synthesis (133,329,331,518). A series of complex reactions takes place when 3-bromothianaphthene is reacted with potassium hydroxide in methanol (329) (eq. 44). Thianaphthene (I) was obtained in about 10% yield while II was the major product. This was identified by conversion to diphenyldisulfide-2,2′-diacetic acid by treatment with methanolic sodium hydroxide. The formation of II probably took place upon acidulation of the potassium salt of *o*-mercaptophenylacetic acid in the isolation procedure. The investigators found this ring closure takes place very easily in the presence of acid. In a second hydrolysis of 3-bromothianaphthene, ethanolic potassium hydroxide was employed under the same conditions as described in eq. 44. In this experiment, thianaphthene (62.5%) and 3-hydroxythianaphthene (15.4%) were obtained, II and III were totally absent.



(44)

(I) (II) (III)

TABLE II-6. Physical Constants of the Halothianaphthenes

Compound	B.p., °C. (mm.)	M.p., °C.	Ref.
3-Cl	96–101 (5) n_D^{20} 1.6390	—	724
5-Cl	85 (4)	—	762
5-Cl, picrate	—	69–70	762
6-Cl	125 (15)	—	762
6-Cl, picrate	—	134	762
7-Cl	115 (10)	—	762
7-Cl, picrate	—	141–142	762
6-Cl-4-CH_3	270 (760) 149–150 (11)	—	378, P-417
2,3-Cl_2	125–127 (10)	55.5–56.5	328, 724
2,3-X,X-Cl_4	175–179 (5)	—	724
2,3,X,X,X-Cl_5	202–208 (5)	111–112	724
2,3,4,5,6,7-Cl_6	—	158	32
2-Br	135–142 (18)	41–42	736
3-Br	269 (752.5)	—	328
	145 (20)	—	78
	136–137 (13)	—	328
	95 (1.5)	—	537
	d_4^{20} 1.6294	—	328

Table continued

TABLE II-6 (*continued*)

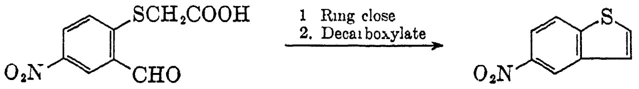
Compound	B.p., °C (mm.)	M p., °C.	Ref.
3-Br, picrate	—	114–115	78, 328
4-Br	Oil	—	747
7-Br	107–109 (10)	—	767
7-Br, picrate	—	144–145	767
2,3-Br_2	—	55.3	327
		58	748
2,3,X-Br_3	—	132	327
2,3,X,X-Br_4	—	229–230	385
2-I	119–120 (1.6)	63.4–65	776
3-I	137–138 (5)	—	327, P-707
	120–121 (1.6)	—	776
	d^{20}_{4} 1.898	—	776
	n^{20}_{D} >1.7	—	776
3-I, picrate	—	107–108	P-707
2,3-I_2	—	60.5–62	540, 748
2-Br-3-Cl	—	60	748
2-I-3-Cl	—	90–92	748
2-CH_2Cl	124–126 (2)	55–56	52
3-CH_2Cl	124–126 (2)	44–45	51a, 27, 90, 533, P-706
3-CH_2SCN	172–176 (2–2.5)	—	724
	n^{25}_{D} 1.6790		
2-Br-3-CH_2Br	—	97.6–98.6	776
3-CH_2CH_2Br	188 (21)	—	90
3-Cl-2-$HgOOCCH_3$	—	188–189	748
3-Cl-2-HgSCN	—	214–215	748
3,3′-Cl_2-2,2′-Hg	—	294–295	748

V. Nitrogen Derivatives

A. Nitrothianaphthenes

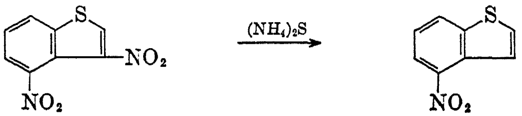
Nitration of thianaphthene was first carried out by Komppa in 1897 (327). At that time he stated that nitration was difficult, but a mononitro derivative, m.p. 77°, could be obtained in glacial acetic acid. This procedure has been repeated twice and the products were described by the two investigators as a solid, m.p. 81° (220), and as a liquid (P-598). Bordwell (private communication to the authors) indicated that a 70% yield of mononitrothianaphthene is obtained by this method but only about 20% of the material can be separated as the pure 3-nitro derivative. The remaining 50% may be a mixture of the 2- and 3-nitro isomers. (*Authors' Note:* The possibility of the 3-nitrothianaphthene dimer should not be overlooked; see eq. 48.) The 2-nitro isomer has not been isolated and identified.

Mononitrothianaphthenes containing a nitro group in the benzenoid ring are prepared by circuitous routes. 5-Nitrothianaphthene is prepared by ring closure (184,60) (eq. 45). Nitration of thianaphthene 1-dioxide yields the 6-nitro isomer (100). 2,3-Dihydrothianaphthene and its 1-dioxide are both nitrated in the 6-position (100).



(45)

4-Nitrothianaphthene is prepared from 3,4-dinitrothianaphthene (eq. 46) by selectively removing the 3-nitro group by reduction (222). This elimination of the nitro group probably proceeds through the amino group, which enolizes and is hydrolyzed to the keto form of 4-nitro-3-hydroxythianaphthene. Reduction of the 3-hydroxythianaphthenes to thianaphthenes is a well-established reaction. 4-Nitrothianaphthene has also been prepared from 5-amino-4-nitrothianaphthene by removal of the amino group by diazotization (747).

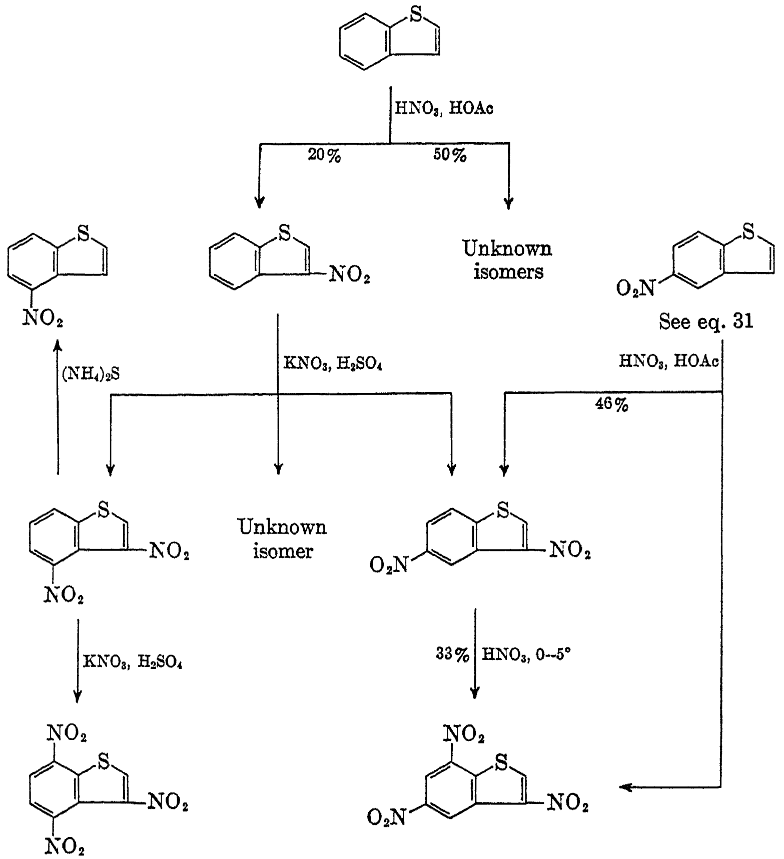


(46)

3,4-Dinitrothianaphthene is the principal product from the nitration of 3-nitrothianaphthene (222,747). In addition, a smaller amount of an isomer that presumably was the 3,5-dinitrothianaphthene and another unknown isomer were obtained. The latter unknown isomer was found to exist in two forms: α, m.p. 98–99°; β, m.p. 119–121°. Nitration of 5-nitrothianaphthene also yields 3,5-dinitrothianaphthene (60).

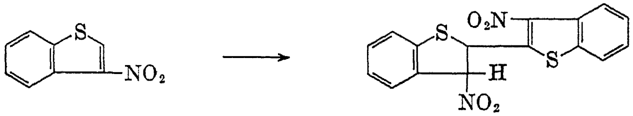
Two trinitrothianaphthenes are known. 3,4,7-Trinitrothianaphthene is said to result from the nitration of 3-nitrothianaphthene or 3,4-dinitrothianaphthene (222). 3,5,7-Trinitrothianaphthene is formed by nitration of 3,5-dinitrothianaphthene. The reaction sequence of eq. 47 is a flow sheet of the nitration reactions of thianaphthene.

The formation of 3,4,7-trinitrothianaphthene from 3,4-dinitrothianaphthene is surprising in view of the fact that the third nitro group is said to enter the benzenoid ring *para* to the 4-nitro group. Since the investigators did not establish the positions of the 4- and 7-nitro groups irrevocably, this work should be reinvestigated.



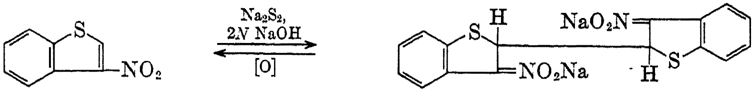
(47)

3-Nitrothianaphthene is apparently a very reactive material, since it dimerizes in acetic acid solution (220) (eq. 48).



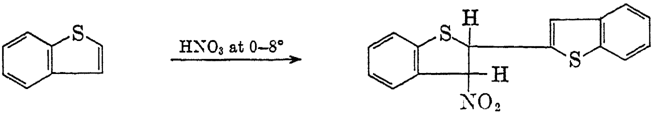
(48)

3-Nitrothianaphthene polymerizes as shown in eq. 49 when basic reduction is attempted (220). The resultant dimeric product is reconverted to the original product by means of oxidizing agents (220).



(49)

It was also noted that thianaphthene when nitrated with nitric acid (dilute or concentrated) gives a product which appears to be a condensation product of thianaphthene with 3-nitrothianaphthene (eq. 50). Komppa (328)



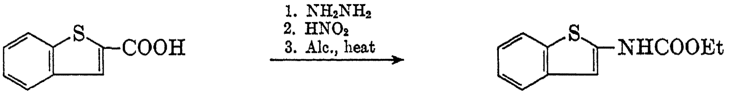
(50)

apparently noted this latter compound and reported that in the nitration of thianaphthene, if insufficient nitric acid was employed, an intermediate, m.p. 154.5°, was obtained.

With the exception of the polymerization reactions (eqs. 48–50) and the reductive replacement of the 3-nitro group by a hydrogen atom (eq. 46), the reactions of the nitrothianaphthenes appear to be similar to those of the benzenoid isologs. Their reduction to aminothianaphthenes will be described in detail in the following section. The tendency of the sulfur atom in thianaphthene to form sulfones is greatly reduced and 3-nitro-, 3,5-dinitro-, and 3,5,7-trinitrothianaphthenes cannot be converted to the sulfones by the usual methods of oxidation (60). It is reported that 3-nitrothianaphthene is brominated in the 2-position but apparently the starting material in the bromination was not pure 3-nitrothianaphthene since it was reported to be a liquid (P-598). Nitration of 3-bromothianaphthene is also said to form 2-nitro-3-bromothianaphthene (P-598), but no structure proof of the product was undertaken. The melting points of the nitrothianaphthenes are listed in Table II-7, p. 52.

B. Aminothianaphthenes

2-Aminothianaphthene is not known. Its ethylurethan derivative has been prepared from 2-thianaphthenecarboxylic acid by rearrangement of the 2-carboxazido intermediate (522) (eq. 51). The structure was established through conversion to the known 2-hydroxythianaphthene by heating in the presence of hydrochloric acid and acetic acid.



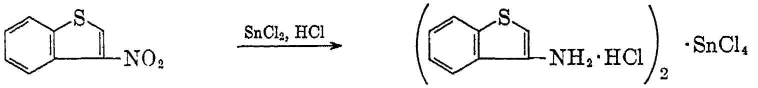
(51)

3-Aminothianaphthene is not stable enough to be isolated in the pure form and is normally obtained in the form of its derivatives. It apparently is even less stable than 2- and 3-aminothiophene, since it is reported that the material cannot be distilled (324). It can be isolated in good

TABLE II-7. Melting Points of Nitrothianaphthenes

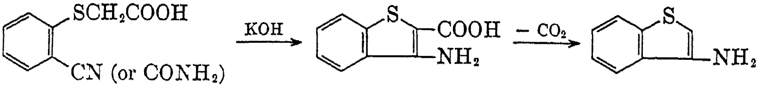
Compound	M p., °C.	Ref.
3-Nitrothianaphthene	77	327
	81	220
	78–79	745
4-Nitrothianaphthene	88	222
	84–85	747
5-Nitrothianaphthene	149–150	184, 60
3,4-Dinitrothianaphthene	199.5	222
3,5-Dinitrothianaphthene	171	60, 222
?,?-Dinitrothianaphthene	α-98–99	222
	β-119–121	222
3,4,7-Trinitrothianaphthene	196	222
3,5,7-Trinitrothianaphthene	196	60
2-Bromo-3-nitrothianaphthene	Brown oil	P-598
3-Chloro-2-nitrothianaphthene	—	748
3-Bromo-2-nitrothianaphthene	160–161	P-598
3-Methoxy-2-nitrothianaphthene	100	748
3-Cyclohexylamino-2-nitrothianaphthene	139–140	748
3-Piperidino-2-nitrothianaphthene	119–121	748

yields as its stannic chloride double salt from the reduction of 3-nitrothianaphthene (328) (eq. 52). This double salt may be used in the preparation of derivatives and the stable acetamido or benzamido derivative may be obtained from a typical Schotten-Baumann type condensation.



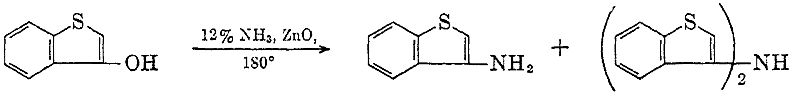
(52)

Another synthesis of this compound involves ring closure typified by eq. 53 (P-298,P-593,P-1,389,P-272,197). Loss of the carboxyl group usually takes place during the ring closure step if sufficiently strenuous conditions are employed. It can also be removed by typical decarboxylation techniques. This ring closure, if accomplished in acidic media, yields 3-hydroxy-2-thianaphthenecarboxylic acid and 3-hydroxythianaphthene. The 3-amino group is easily replaced by the hydroxyl group in the presence of acid. This reaction is reversible and 3-aminothianaphthene (I) and di-(3-thianaphthenyl)amine (II) can be obtained by condensation of 3-



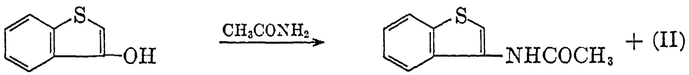
(53)

hydroxythianaphthene with ammonia when zinc oxide is employed as a condensing catalyst (324) (eq. 54). Ammonium sulfite, as well as dilute ammonia alone, with 3-hydroxythianaphthene gives similar results. I is almost completely converted to II in aqueous alkaline solution (222,324). II results even when 3-hydroxythianaphthene is treated with acetamide in acetic acid (324) (eq. 55). II is the principal product when long reaction periods are employed.



(I) (II)
10%

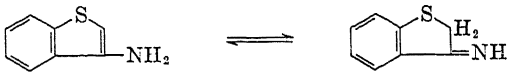
(54)



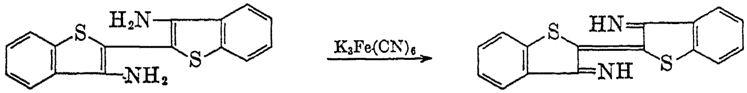
30%

(55)

The instability of 3-aminothianaphthene probably is due to its ability to exist in two forms, the amino form and the tautomeric imino form, the latter contributing greatly to its instability (eq. 56). In contrast, 3,3′-diaminobithianaphthene (III) prepared by reduction of the 3,3′-dinitro derivative with stannous chloride in acetic acid is a much more stable compound and can be oxidized to the corresponding 3,3′-diiminothioindigo, IV (220) (eq. 57). The diacetamido derivative of III can also be oxidized to the diacetamido derivative of IV. IV gives a violet-colored monohydrochloride salt when treated with concentrated alcoholic hydrogen chloride. 3-Amino-2-(3′-thianaphthenyl)-2,3-dihydrothianaphthene, prepared in the same manner as III above, is also stable as the free base, as is 3,3′-diamino-2,2′,3,3′-tetrahydrobithianaphthene. The latter



(56)

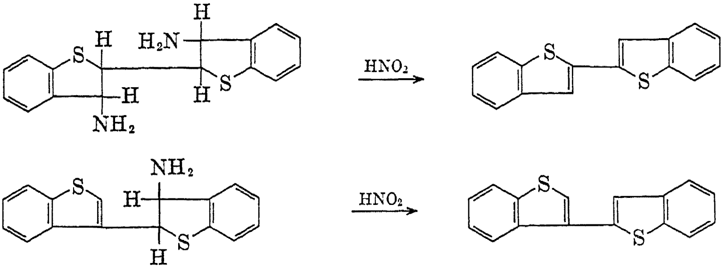


(III)
Yellow, m.p. 238°

(IV)
Orange-red, m.p. 228° (dec.)

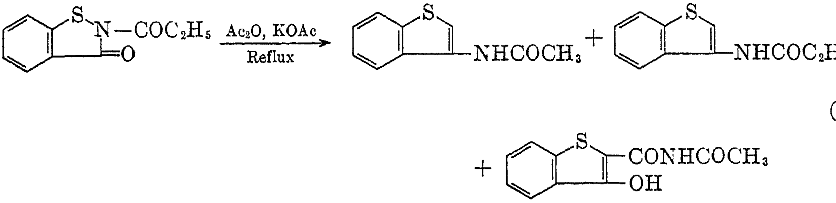
(57)

two compounds, when treated with nitrous acid, are reported to yield the corresponding bithianaphthenes rather than the expected dihydrobithianaphthene derivatives (220) (eq. 58).

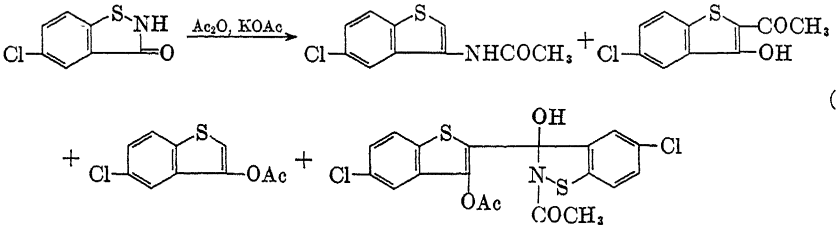


(58)

Amides of 3-aminothianaphthene are obtained when *N*-propionamidobenzoisothiazole is treated with acetic anhydride and potassium acetate (361,191) (eq. 59). When *N*-phenylacetamidobenzoisothiazole is employed, the corresponding 3-phenylacetamidothianaphthene can be obtained as one of the products of the reaction (361). 5-Chloro-3-acetamidothianaphthene is obtained as shown in eq. 60 (191). This ring closure is

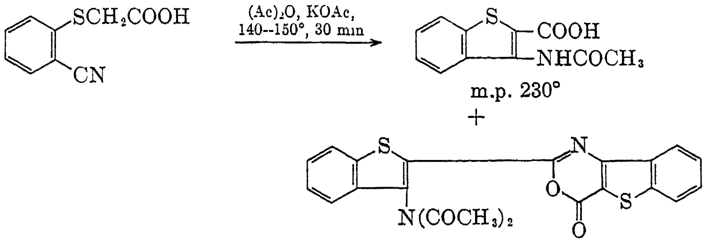


(59)



(60)

discussed more thoroughly in section VI. Other 3-aminothianaphthene derivatives are obtained by the action of acetic anhydride and potassium acetate on *o*-cyanophenylthioglycolic acid (363) (eq. 61). V with 90% acetic acid yields the monoacetyl derivative, VI, m.p. 312°, which is reconverted to V with acetic anhydride. VI and propionic anhydride yields the *N*-acetyl-*N*-propionyl derivative, m.p. 230°. V with 5% alcoholic

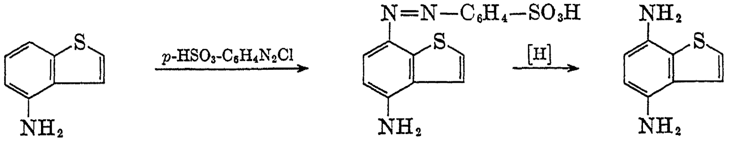


(V)
Yellow
m.p. 259°

(61)

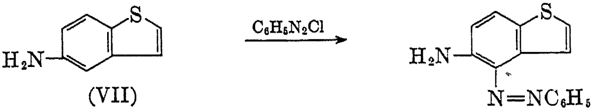
sodium hydroxide or with sulfuric acid at 70° gives the corresponding stable 3-amino derivative, m.p. 246°. Other complex derivatives of V are listed in the original article (363).

Aminothianaphthenes with the amino group in the benzenoid ring are more stable than the 2- or 3-aminothianaphthenes. Their physical constants are listed in Table II-8. With the exception of 4,7-diaminothianaphthene, members of this class of amines are prepared by standard procedures from their corresponding nitro or dinitro compounds (184,222, 60). 4,7-Diaminothianaphthene is prepared from 4-aminothianaphthene by coupling and subsequent reduction of the azo compound (222) (eq. 62).



(62)

5-Aminothianaphthene (VII) couples in the 4-position (eq. 63), but the diazo derivative is not reduced to the corresponding diamine derivative (222). Compound VII brominates in the 4-position to yield 5-amino-4-



(VII)

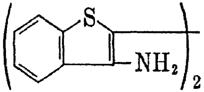
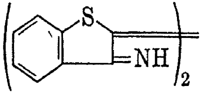
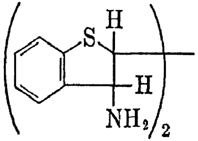
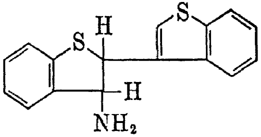
(63)

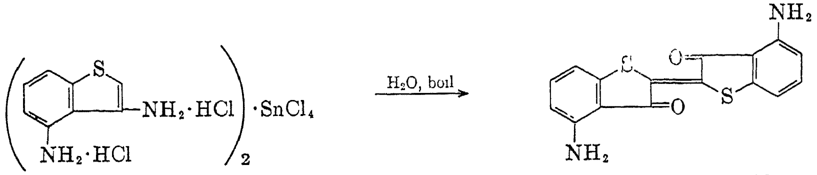
bromothianaphthene. For details of the Skraup synthesis and acridine synthesis see Chapter VIII (section III-b).

3,4-Diaminothianaphthene is easily converted to 4,4′-diaminothioindigo by refluxing its stannic chloride double salt in water (222) (eq. 64, p. 58).

TABLE II-8. Aminothianaphthenes and Their Derivatives

Compound	M.p., °C.	Deriv.	M p., °C.	Ref.
2-Amino-	—	Ethylurethan	161	522
3-Amino-	—	5-Chloro-3-acetamido	208–210	191
		2-Bromo-3-propionamido	156	361
		2-Nitro-3-benzamido	180	361
	—	$(3\text{-}C_8H_6SNH_2\cdot HCl)_2SnCl_4$	204	328
		Acetamido-	169	220,328,197,324
		Benzamido-	132	328
		3-Thianaphthenyl	114	324,220
		3-Propionamido	115	361
		Phenylacetamido	76	361
		2-Nitrophenylacetamido	181	361
4-Amino	59	Acetamido	134	222
	51–53			747
5-Amino	72		—	222,60,184
		Acetamido	106	222
		3-Bromo-	84	60
		N,*N*-Diethyl	B.p. 168–171 (0.5 mm.)	60
		4-Bromo	75	222,747
		4-Bromo-acetamido	143	222,747
		$4\text{-}N{=}N\text{-}C_6H_5$	103	222
		$\text{Acetamido-}4\text{-}N{=}N\text{-}C_6H_5$	154	222
		Benzylidene anil	98	222
		4-Nitro	190	747
		4-Nitroacetamido	131–132	747

Compound	M.p., °C.	Deriv	M.p., °C.	Ref
3,4-Diamino	167			222
4,7-Diamino	114	Di-HCl	151 (dec.)	222
		Diacetamido	287	222
	238	Diacetamido	285	220
	228 (dec.)	Diacetimido	—	220
	83.5	Diacetamido	231	220
	271	HCl	298 (dec.)	220
		Acetamido	225	220



(64)

Ultramarine to marine blue

5-Aminothianaphthene appears to be the only compound of this class to be tested for bacteriostatic action. It is said to inhibit growth of turbercular organisms (54).

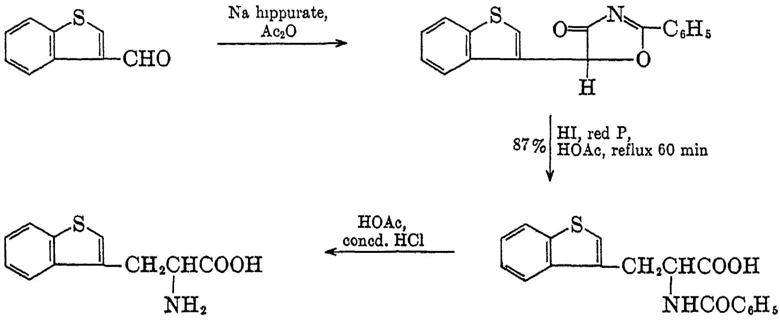
The melting points of this class of compounds and their derivatives are tabulated in Table II-8.

C. Derivatives with Nitrogen in a Side Chain

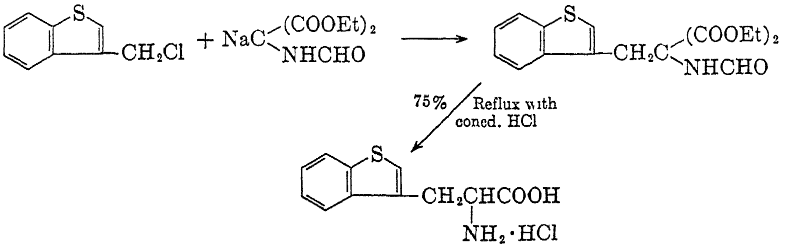
Study of this class of compound is very limited. This is reminiscent of this thiophene class prior to the advent of the antihistaminic compounds. Apparently, no attempt has been made to prepare the sulfur analog of gramine, or to investigate the possibility that thianaphthene will undergo the Mannich reaction.

A series of substituted 2-aminomethylthianaphthenes have been synthesized by reduction of the respective substituted 2-thianaphthenecarboxamides with lithium aluminum hydride (736). These compounds and their physical properties are listed in Table II-9.

Two syntheses of 3-thianaphthenylalanine have been announced. One synthesis involves the usual condensation of 3-thianaphthenecarboxaldehyde, sodium hippurate, and acetic anhydride to produce 2-phenyl-4,3′-thianaphthenylmethyleneoxazol-5-one. This is then reduced and saponified to yield 3-thianaphthenylalanine (176) (eq. 65). The second method proceeds by the well-known malonic acid synthesis employing diethyl *N*-formyl aminomalonate (27) (eq. 66).



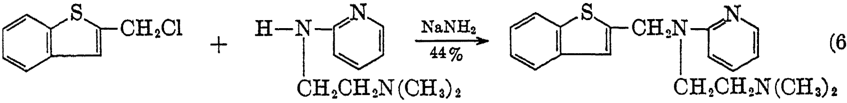
(65)



(66)

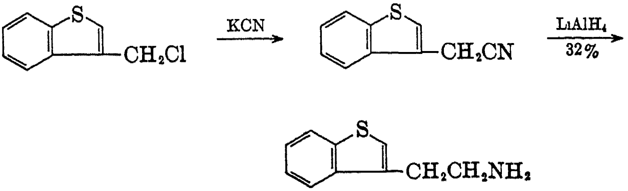
The action of 3-thianaphthenylalanine against the organism *Lactobacillus arabinosus* 17–5, indicated an inhibitor metabolite ratio of 250 at 1:10,000 dilution (compared to 5-methyl-DL-tryptophane with an inhibitor metabolite ratio of 2500) (27). This compound is also an effective growth inhibitor for the organism *Streptococcus hemolyticus* in broth at dilution of 1:20,000.

Blicke and Sheets (52) have prepared a few amine compositions isologous to those showing antihistaminic activity in the thiophene series, but the data for physiological action have not yet been reported. Thus both the 2- and 3-thianaphthene analogs of Pyrabenzamine have been prepared as shown in eq. 67. Both the 2- and 3-isomers of *N*-phenyl-*N*-(dimethylaminoethyl)aminomethylthianaphthene have been prepared by this synthesis (52). The 3-isomer of I was also prepared by reacting 3-chloromethylthianaphthene first with 2-aminopyridine and then with dimethylaminoethyl chloride (51a).



(67)

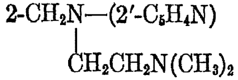
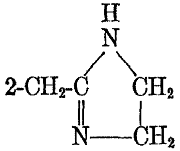
2-(3'Thianaphthenyl)ethylamine is conveniently prepared from 3-chloromethylthianaphthene by the following sequence of reactions (608)

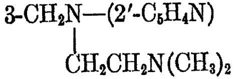
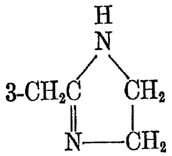
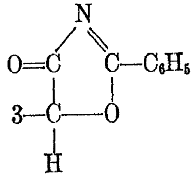


(68)

(eq. 68). In addition a small amount of 2-(3′-thianaphthenyl)ethanol is said to form in the reduction. The amine formed a dipicrate; the *N*-

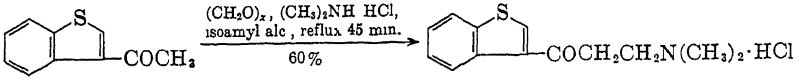
TABLE II-9. Physical Properties of Thianaphthene Derivatives with Nitrogen in the Side Chain

Thianaphthene substituted at X-position with	B p., °C. (mm.)	Deriv.	M p , °C.	Ref
$2\text{-}CH_2NH_2$	M.p. 58–59	—	—	736
$2\text{-}CH_2NHC_6H_5$	M.p. 113–113 5	—	—	736
$2\text{-}CH_2NH{-}C_6H_4\text{-}o\text{-}CH_3$	M.p. 69–69 5	—	—	736
$2\text{-}CH_2NH\text{-}2\text{-}C_5H_4N$	M.p. 121 5–122	—	—	736
$2\text{-}CH_2NH\text{-}2\text{-}C_3H_3NS$	M.p. 149 5–150	—	—	736
$2\text{-}CH_2N(C_6H_5)CH_2CH_2N(CH_3)_2$	185–188 (0 02)	HCl	183–184	52
 $2\text{-}CH_2N(2'\text{-}C_5H_4N)CH_2CH_2N(CH_3)_2$	175–180 (0 02)	HCl	149–150	52
	—	HCl	274–277 (dec.)	51a
$3\text{-}CH_2CH_2NH_2$	125 (1)	Dipicrate	176 5–177 (dec.)	608
		$N\text{-}CH_3CO$	68	
		$N\text{-}C_6H_5CO$	93	
$3\text{-}CH_2C(CH_3)_2NH_2$	—	HCl	229	90
$3\text{-}CH_2CH_2C(CH_3)_2NH_2$	—	HCl	219	90
$3\text{-}CH_2C({=}NH)OC_2H_5$	—	HCl	103	51a
$3\text{-}CH_2N(C_6H_5)CH_2CH_2N(CH_3)_2$	162–165 (0 1)	HCl	199–200	52

Thianaphthene substituted at X-position with	B.p., °C. (mm.)	Deriv.	M.p., °C.	Ref.
3-CH_2NH-(2′-C_5H_4N)	180–185 (1)	HCl	101–103	51a
3-$CH_2N(C_2H_5)CH_2CH_2OH$	—	HCl	129–130	P-706
3-$CH_2N(C_2H_5)CH_2CH_2Cl$	—	HCl	147–148	P-706
 3-CH_2N—(2′-C_5H_4N) $CH_2CH_2N(CH_3)_2$	169–170 (0 01)	HCl	186–187	51a,52
	—	HCl	234–235	51a
	M.p. 219–220	—	—	176
3-$CH_2CH(NH_2)COOH$	M.p. 248–250 (dec.) M.p. 279–280	*N*-COC_6H_5	—	176 27
3-$COCH_2CH_2N(CH_3)_2$	—	HCl	175–176	52
3-$CH_2OCH_2CH_2N(CH_3)_2$	125–127 (0 5)	HCl	132–135	52

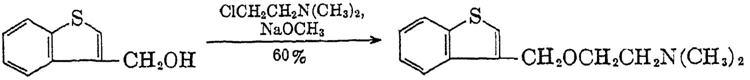
acetyl and *N*-benzoyl derivatives were formed and converted to the corresponding isoquinoline derivatives (see Chapter VIII).

3-(β-Dimethylaminopropionyl)thianaphthene has been synthesized from 3-acetylthianaphthene via the Mannich reaction (52) (eq. 69).



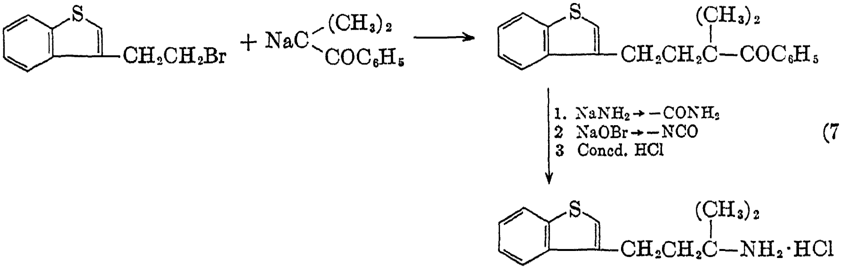
(69)

3-Thianaphthenylmethyl dimethylaminoethyl ether has been made in the following manner from 3-thianaphthenylcarbinol (52) (eq. 70).



(70)

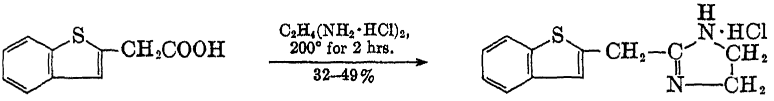
Cagniant (90) has prepared a series of branched-chain alkyl amines by a rather unusual synthesis. Shown in eq. 71 are the steps involved in the synthesis of 1-(3-thianaphthenyl)-3-amino-3-methylbutane from 3-(2′-bromethyl)thianaphthene. 1-(3-Thianaphthenyl)-2-amino-2-methylpropane is prepared from 3-chloromethylthianaphthene in the same manner.



(71)

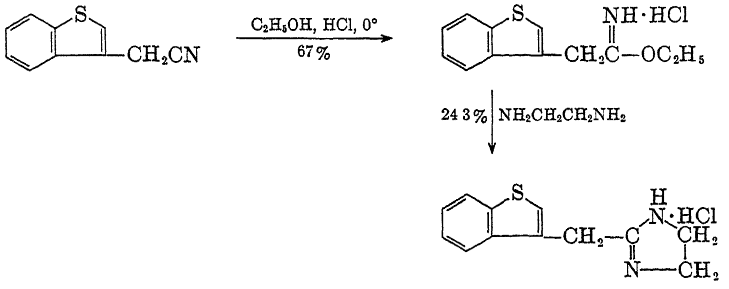
Table II-9 lists the physical constants of this series of compounds and some of their derivatives.

The isomeric 2-(2′- and 3′-thianaphthenyl)methylimidazolines are obtained by heating the respective thianaphtheneacetic acids with anhydrous ethylenediamine hydrochloride (51a) (eq. 72). Somewhat lower



(72)

yields are reported when the acetate esters are employed In addition, the 3-isomer was synthesized by the method of eq. 73 (51a). Fully aromatic nitrogen heterocycles of this series are discussed in part I*C* of this chapter, and the physical properties are tabulated in Table II-3.



(73)

VI. Hydroxythianaphthenes (Thianaphthenols or Thioindoxyls)

The hydroxythianaphthenes and thianaphthenequinones are the most familiar thianaphthene derivatives, and are the only ones to have commercial applications. They are intermediates for the preparation of thioindigo dyes. Much research has been devoted to synthetic methods, particularly those leading to intermediate phenylthioglycolic ("phenylmercaptoacetic" in *Chemical Abstracts*) acids. Only a few of the simpler examples are included in this book. However, in tribute to those anonymous industrial chemists whose work for the German and Swiss dye industries lies buried in obscure patent literature, it must be said that their systematic study in preparing nearly every possible isomeric halogen-substituted methylhydroxythianaphthene from the intermediate substituted phenylthioglycolic acids is such that a modern textbook written on this subject alone would be a model for the preparation of positional isomers in any aromatic or heterocyclic series.

Not all of the hydroxy derivatives of thianaphthene are discussed in this section. In compiling this chapter, the hydroxyl group has been subordinated to aldo, oxo, carboxyl, and sulfone functional derivatives. The syntheses of derivatives containing these groups are discussed, and the physical constants are listed in those sections.

The nomenclature chosen for the larger part of this section is the same as that appearing in the original literature and differs from that now used by *Chemical Abstracts.* Thus the term hydroxythianaphthene and occasionally the term thioindoxyl are used in place of 3-thianaphthenol and 2,3-dihydrothianaphthen-3-one.

A. Tautomerism of 2- and 3-Hydroxythianaphthenes

The subject of tautomerism of the hydroxythianaphthenes has been discussed at great length, but few concrete conclusions have been reached. The experimental work was carried out several decades ago and the chemical methods used to establish the relative ratio of tautomers were incapable of yielding concise data. The application of recently developed spectrophotometric techniques to this problem would undoubtedly give a clearer and truer picture of the ratio of tautomers present.

After having studied the chemical properties of 3-hydroxythianaphthene, Friedlander recognized the similarity of this compound and its isostere, indoxyl. Since the majority of these reactions involved the keto form, he used the name thioindoxyl to describe its properties. Since the reactions of the keto form became the most important and best known, the older literature almost always represented the compound in the keto or oxo form, *i.e.*, as 2,3-dihydrothianaphthen-3-one. However, early workers recognized that methyl sulfate converted the compound to the methoxyl derivative and found that it could be coupled in the 2-position with diazonium salts to yield typical azo derivatives. Also, they recognized that esters could be formed from both the sodium salt or free hydroxyl group in boiling acetyl chloride.

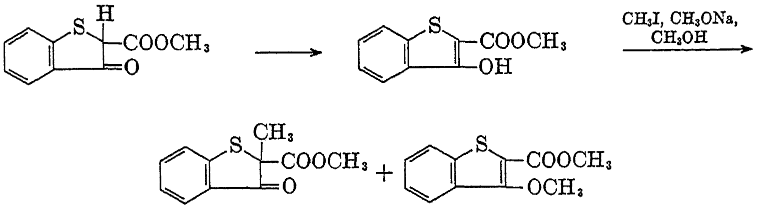
Auwers and Theiss (23), in attempting to establish the structure of the material in the solid state, were forced to conclude that their inadequate methods, which involved a bromine titration, led to only 1 to 5% of the enol form. Admittedly, very exact values could not be obtained due to a variety of complicating and uncontrollable factors. They did conclude, however, that the "hydroxythianaphthenes" in the solid state appeared to be true ketones, and that the preferred designation should be thianaphthenones or thioindoxyls. Their study indicated that compounds of this class were similar to the coumarones in reactions in that they easily react as enols both in the free state and in alkaline solution, while compounds of the hydrindone series do not. On the other hand, they resemble the hydrindones and differ from the coumarones in that their 5-membered ring apparently cannot be ruptured by ketonic reagents. These three classes of compounds readily undergo autoxidation, a property common to the keto form. The resultant products in the thianaphthene series are, of course, the thioindigo dyes which are discussed in detail in Chapter III.

Marschalk (370,371), in studying the properties of the very unstable 2-hydroxythianaphthene, found that the material existed in two solid forms. When prepared from *o*-mercaptophenylacetic acid by dehydration with phosphorus pentoxide, the enol form, m.p. 44.5°, was obtained.

When obtained from the same compound by dehydration with acetic anhydride, the keto form m.p. 33–34° was isolated. Distillation converted the enol form to the keto form. The enol form was also obtained by dissolving the keto form in cold sodium hydroxide followed by acidification. The enol form was distinguished from the keto form by the blue color produced with ferric chloride.

Apitzsch (13) has noted that 2-(*p*-nitrophenyl)-3-hydroxythianaphthene also exists in both tautomeric forms. He describes a red enol form that is obtained in recrystallization of the product from water, a yellow keto form that is obtained from acetic acid, and an orange-red mixture. This compound, as the sodium salt, forms pure blue crystals; it is cherry red in water and in sodium bicarbonate solution, but blue in pyridine solution. In amine solution, it is red-violet to blue with the exception of aniline solution, in which it is colorless.

Auwers (20,21) has indicated that when methyl 3-hydroxy-2-thianaphthenecarboxylate is treated with sodium methoxide and methyl iodide two compounds are formed; one form is the normal methoxyl derivative and the other is the C-methylated compound of the keto form (eq. 74).

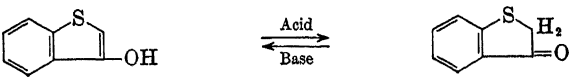


(74)

However, Auwers indicated that only the normal methoxyl derivatives could be obtained if the methylation is carried out with dimethyl sulfate.

Auwers and Arndt (18), reporting on the properties of 5-methyl-3-hydroxythianaphthene, describe it as a white crystalline material which, when moist, becomes yellow but changes slowly to a carmine-red color. In alkali solution a blue color develops very slowly.

It is evident from the foregoing discussion that more experimentation with modern techniques and spectrophotometric analyses is needed to clarify this problem. At the present time, one must conclude that both forms exist and that the compounds should be represented as existing in a tautomeric state (eq. 75). While the equilibrium is shown with acid favor-



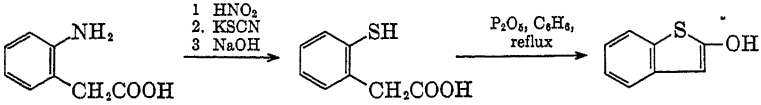
(75)

ing the keto form, and base favoring the enol form, reactions listed below indicate that both forms may react in either basic or acidic media. *Note added in proof:* In this connection, a recent ultraviolet absorption investigation of the structure of 3-hydroxythieno[3,2-*b*]pyridine indicated that the compound existed entirely in the enol or hydoxy form (771).

B. Preparation of Hydroxythianaphthenes

1. 2-Hydroxythianaphthenes

2-Hydroxythianaphthene is isolated in its enol form, m.p. 44.5°, by a series of reactions starting from *o*-aminophenylacetic acid. The final dehydration step with *o*-mercaptophenylacetic acid is effected by phosphorus pentoxide (370,371) (eq. 76). The thioindoxyl (keto) form, m.p. 33–34°, is said to be formed by ring closure of the *o*-mercaptophenylacetic acid with acetic anhydride(370,371) or by steam distillation in the presence of hydrochloric acid (329) (eq. 77). It is also formed by rearrangement of the enol form through distillation (370) or by recrystallization (329). The keto form is rearranged to the enol form by treating with cold dilute caustic followed by acidification.



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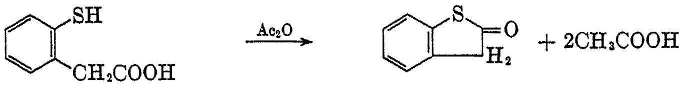
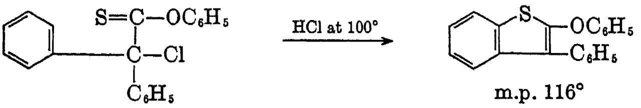


(77)

A compound reported to be 2-phenoxy-3-phenylthianaphthene has been prepared by the ring closure of phenyl chlorodiphenylacetothionate (444) (eq. 78). The 2-thiophenyl derivative (m.p. 123°) was also obtained by this method. 2-Phenoxy-3-*p*-tolyl-6-methylthianaphthene (m.p. 102°) was synthesized from phenyl chlorodi-*p*-tolylacetothionate. (These thionoesters are prepared by condensation of phenoxythiocarbonyl chloride and diphenyl-(or di-*p*-tolyl) acetonitrile.)

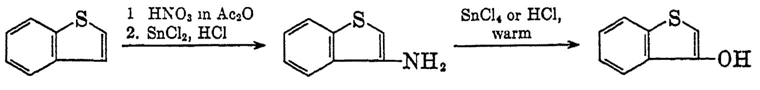


(78)

2. 3-Hydroxythianaphthenes

(a) From Thianaphthene

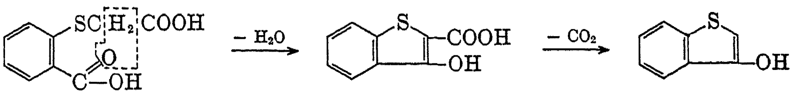
Fries and Hemmecke (220) first prepared 3-hydroxythianaphthene from thianaphthene by means of a multiple-step synthesis involving the 3-amino derivative (eq. 79). The overall yield was not high but was better than the 7.7% yield obtained by Komppa (329) from oxidation of 3-thianaphthenylmagnesium bromide.



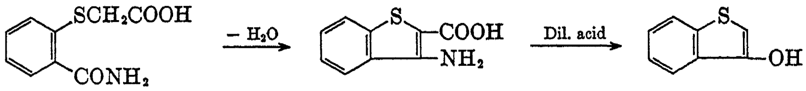
(79)

(b) By Ring-Closure Methods

The best methods for preparing 3-hydroxythianaphthenes require ring-closure syntheses. The most common of these is the cyclization of *o*-carboxyphenylthioglycolic acids by means of a variety of condensing agents (for details see Table II-10). Most of the methods are concerned with condensation of the methylene group of the thioglycolic moiety with the *ortho*-carbonyl group (eq. 80). When the *o*-carboxy group is replaced by a carboxamide group, the intermediate is a 3-amino-2-carboxy derivative. This can be decarboxylated by heat and the resultant 3-amino derivative can be hydrolyzed to 3-hydroxythianaphthene, or the intermediate may be decarboxylated and the amine group hydrolyzed simultaneously by means of dilute mineral acid (eq. 81).

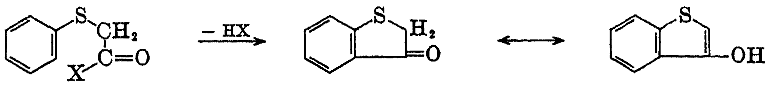


(80)



(81)

Another widely used synthesis proceeds by ring closure of a phenylthioglycolic acid by means of strong acids or Friedel-Crafts catalysts (eq. 82).



X = Cl or OH

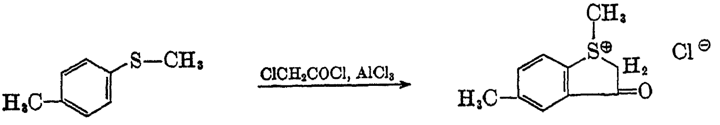
(82)

TABLE II-10. Methods of Preparing 3-Hydroxythianaphthenes

Starting compound	Condensing agent and conditions	Ref.
o-Carboxyphenylthioglycolic acids or their mono or diesters	1. Fuse with KOH or NaOH at 180–200°	195,197,208,P-234,P-268
	2. Hydrolyze with mineral acid	P-274,P-288a,P-292,P-293, P-295,P-340
	73% aq. H_2SO_4 in presence of $KHSO_4$, H_3PO_4, or H_3BO_3; heat	P-374,P-375
	$(CH_3)_2SO_4$, 100°	573,574
	Acetic anhydride above 100°	P-302,P-327,23,520,P-234, P-268,P-288,P-441,P-443,P-461
	Water at 100–250°, preferably 180°	P-535
	Aq. NaOH and Na_2CO_3 at 80°	P-538
	Heat at 170° for 4 hrs.	P-269,P-634
o-Cyano (or carboxamido) phenylthioglycolic acids	1. Reflux with acetic anhydride	P-1,P-441–443
	2. Saponify 3-hydroxyester with alkali	P-455,P-461,P-76,454,295
	Heat with water at 180°	P-189,P-420,P-535
	1. Fuse with caustic	P-1a
	2. Hydrolyze with 60° Bé. H_2SO_4	P-270,P-272,P-298,P-299,P-530
	Heat with H_2SO_4	P-77
	Heat with aq. NaOH and Na_2CO_3	P-88,P-184,P-187,P-635
	Heat with acetic anhydride and CH_3COOK	363,364
Phenylthioglycolic acids	$ClSO_3H$ below 0°	295,416,423,P-19,P-331,P-446
	FSO_3H	P 403,P-524
	HF	505
	1. Acetic anhydride	23
	2. NaOH	
	P_2O_5; heat above 200°	266,P-328
	P_2O_5 on silica; reflux in benzene solvent	P-637
	1. $SOCl_2$ or PCl_3	23,P-440,P-574
	2. $AlCl_3$	P-136
	H_2SO_4 (end product was thioindigo)	P-60

Starting compound	Condensing agent and conditions	Ref.
Methyl phenyl sulfide	$ClCH_2COCl$, $AlCl_3$	18,504,505,573,574
o-Carboxyphenyl methyl sulfides	Fuse with alkali or alkaline earth hydroxides or alcoholates	P-6,P-291,P-302,P-487–495
	Heat with disodium cyanamide	P-296
	Heat with excess chloroacetic acid	574
	Fuse with lead-sodium alloy	P-302
o-Mercaptobenzoic acid	Malonic acid, H_2SO_4, 55°	304,414
	Ethyl acetoacetate, concd. H_2SO_4 at 28–30°	461
	Pyruvic acid, concd. H_2SO_4	283
	Acetyl pyruvic acid, concd. H_2SO_4	283
	Hydroxymaleic acid, concd. H_2SO_4	283
2,2′-Dithiobenzoic acids or their amides	Acetic anhydride and CH_3COOK	34,190
	Heat with ethyl acetoacetate	284
	Sodium trithionate (Na_2CS_3); product is 2,2′-thioindigo	P-411
Benzoisothiazoles	Acetic anhydride, CH_3COOK reflux	35,191,359,361
o-Thiocyanatoacetophenone	Alc. KOH	14
o-Benzylthiobenzoic acids	Sodium methoxide in boiling methanol; products are 2-phenyl derivatives	13,311,358,427

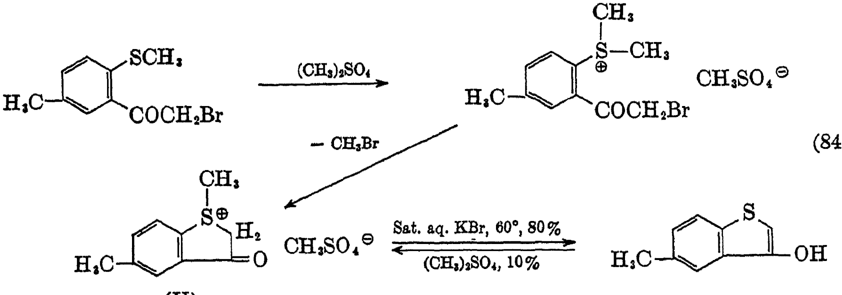
One of the most interesting syntheses of this class is the condensation of chloroacetyl chloride with methyl phenyl sulfides (thioanisoles) in the presence of aluminum chloride (18,504,505). Krollpfeiffer and coworkers (573,574) have shown that this synthesis proceeds through an intermediate sulfonium derivative which has been isolated, characterized, and converted to the expected end product (eq. 83). In this case, equimolar amounts of aluminum chloride were used. Use of 1.25 moles yielded the expected end product, 5-methyl-3-hydroxythianaphthene. Compound I reacted with picric acid to yield a "thianaphthenium picrate," $C_{10}H_{11}OS \cdot C_6H_2(NO_2)_3O$ (m.p. 154–155°) through elimination of hydrogen chloride. Subsequent treatment of this sulfonium salt with hydrochloric acid yielded 5-methyl-3-hydroxythianaphthene.



(I)

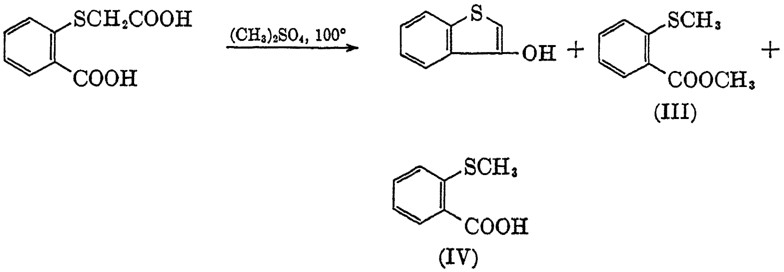
(83)

The following equations also illustrate the role of sulfonium salts in this cyclization (573) (eq. 84). Further evidence for a sulfonium salt intermediate was obtained from a study of the products from the ring closure of *o*-carboxyphenylthioglycolic acid with dimethyl sulfate (574) (eq. 85). The thioanisole derivatives, III and IV, found in the reaction mixture were said to have resulted from disproportionation of an intermediate sulfonium salt, although they could have occurred by decarboxylation. It was also found that if IV was heated with excess chloroacetic acid, in the absence of catalysts, the corresponding 2-carboxy-3-hydroxythianaphthene, V, was obtained in good yield. Again this was thought to occur through an



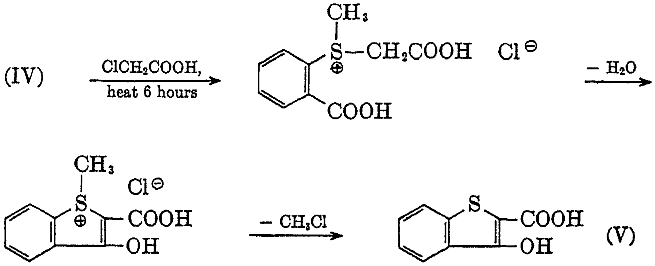
(II)

(84)



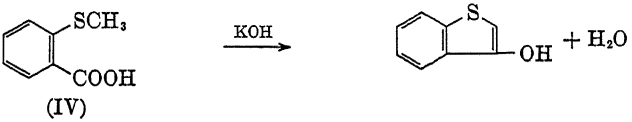
(85)

intermediate sulfonium salt which decomposed to yield methyl chloride and V (eq. 86).



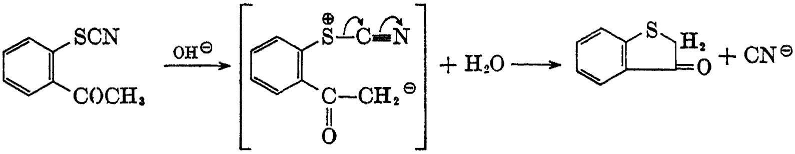
(86)

o-Carboxyphenyl methyl sulfide can also be cyclized by alkali to yield 3-hydroxythianaphthene. Although this reaction is somewhat similar to the previous one, it obviously does not involve a sulfonium intermediate:



(87)

A synthesis, involving the active methylene hydrogens of *o*-thiocyanatoacetophenone, is reported. This reaction probably takes place through an attack of a hydroxyl ion on the methyl radical of the ketone group followed by a 1,4-addition reaction (eq. 88). Another method involving an aceto-



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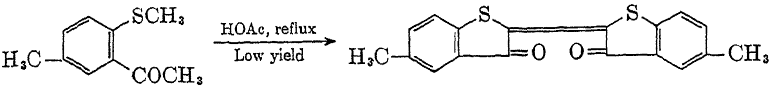
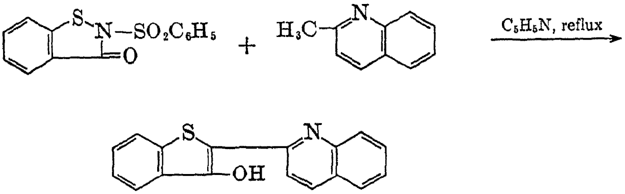


(89)

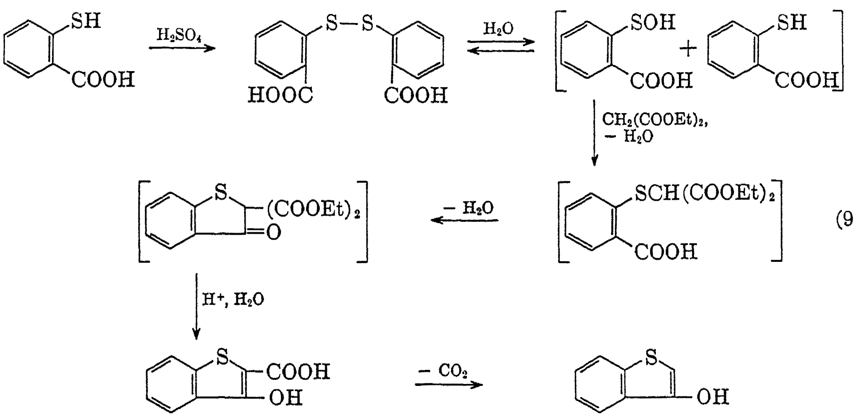
phenone derivative forms 5,5′-dimethylthioindigo from 5-methyl-2-methylthioacetophenone (335) (eq. 89). The intermediate, 5-methyl-3-hydroxythianaphthene, could not be isolated.

McClelland and coworkers (18,35,311,358,427) have developed a synthesis that utilizes benzoisothiazoles as intermediates. In addition to the hydroxythianaphthenes, which are obtained only as one of several products, oxo and amino derivatives of thianaphthene are formed. For further details of this reaction see sections V-b and VIII-b. This reaction requires compounds containing active methylene groups and can be extended to the active methylene groups of the pyridine and quinoline series (35). For example, quinaldine yields ruby-red 2-(2′-quinolyl)-3-hydroxythianaphthene, while α-picoline yields fawn-colored 2-(2′-pyridyl)-3-hydroxythianaphthene. The reaction is illustrated with quinaldine (eq. 90). Both compounds are reported to form acetyl derivatives.



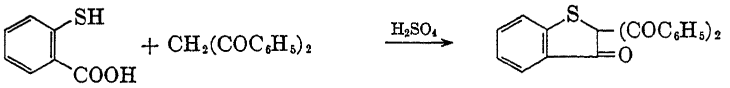
(90)

Smiles and coworkers (460,461,414,304,283) studied the reaction of *o*-mercaptobenzoic acid with compounds containing active methylene groups in sulfuric acid solution. This was found to be a convenient synthesis for 3-hydroxythianaphthene, although a considerable amount of by products, including thioindigo, was usually formed in the reaction. Several examples of this synthesis are given in Table II-10. Smiles came to the conclusion that the principal reaction proceeded by oxidation of the aromatic thiol to the disulfide (by air or sulfuric acid), which acted in sulfuric acid solution as an equilibrium mixture of the mercaptan and sulfenic acid. The sulfenic acid was felt to be responsible for the condensation with the reactive methylene groups as illustrated by eq. 91. In most cases the intermediate 2,2-dicarbethoxy derivative could not be isolated. However



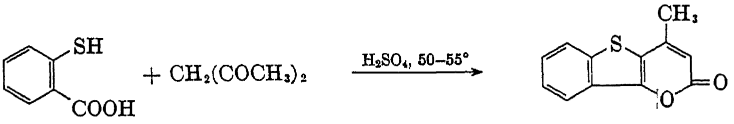
(91)

Smiles and Ghosh (460) were successful in obtaining stable 2,2-dibenzoyl-3-hydroxy-2,3-dihydrothianaphthene by employing dibenzoylmethane (eq. 92). The investigators described their product as a brown crystalline material, m p. 79°. It gave a brown color with ferric chloride, yielded 3-hydroxythianaphthene when fused with caustic, and thioindigo when treated further with sulfuric acid.



(92)

Acetylacetone condenses with *o*-mercaptobenzoic acid to yield a condensed pyran derivative of thianaphthene (eq. 93) (see also Chapter VII, section II-b). This pyran derivative results in quantitative yield when 3-hydroxythianaphthene is treated in a similar manner with acetylacetone.



(93)

3. *4-Hydroxythianaphthenes*

4-Hydroxythianaphthene was the first compound containing the thianaphthene ring system to be reported. Biedermann (49,388) recognized the condensation product of 2-thiophenealdehyde and disodium succinate

TABLE II-11. Physical Constants of the Hydroxythianaphthenes

Position of hydroxyl group	Ref.	M.p., °C.	Deriv.	M.p., °C.	Ref.
2-OH..........	329,370,371	*Keto* form 44 5	Azine	128	371
		Enol form 34–34 5			
		B.p. 260–264 (733 mm.)			
3-OH..........	35,195,197	71	Methoxy	B.p. 148 (20 5)	20
	52	B.p. 95–100 (1 mm.)		$d_4^{13\ 6}$ 1 2093	20,22
				n_D^{20} 1.6248	20,22
			Ethoxy	B.p. 154 (19)	20
				$d_4^{17\ 6}$ 1 1591	20,22
				n_D^{20} 1 6040	20,22
			Acetate	B.p. 165 (18)	23
				$d_4^{20\ 4}$ 1 2580	23
				n_D^{20} 1 60464	23
			Carbonyl ester	123–125	P-371
			Glucoside	73 5	131
			Tetracetylglucoside	106	131
			—OCH_2COOH	160–161	52
			—OCH_2COOCH_3	49–50	52
			—OCH_2CH_2COCl	164	335

Position of hydroxyl group	Ref.	M.p., °C.	Deriv.	M.p., °C.	Ref.
3-OH			3-Anil	67	216
			3-Semicarbazone	224–226	23
			3-*p*-Nitrophenylhydrazone	205	23
			2-Chloro	Red oil	46,P-314
			2,2-Dichloro	Yellow oil	P-341
			2-Bromo	89	46,P-341
			2,2-Dibromo	133	46,P-341
4-OH..........	49,338	72	OCH_2COOH	152–153	184
	184	80–81			
	747	78–79			
5-OH..........	184,222	103–104	Methoxy	44	222,763
			Ethoxy	B.p. 145 (12 mm.)	763
			Ethoxy, picrate	93	763
6-OH..........	—	—	Methoxy	B.p. 153–156 (16 mm.)	763
			Methoxy, picrate	105–106	763
7-OH..........	763	67–68	Methoxy	B.p. 140–145 (15 mm.)	763
		B.p. 135 (18 mm.)	Methoxy, picrate	110–111	763
			Picrate	184–186	763

TABLE II-12. Physical Constants of the Substituted 3-Hydroxythianaphthenes

Substituents	Ref.	M.p., °C.	Hydroxyl deriv.	M.p., °C.	Ref.
2-CH_3	359	Oil	Acetate ester	B.p. 168–170 (25)	427
				75	
4-CH_3	140,P-77,P-447,	65–68			
	274	75–76			
5-CH_3	18,140,P-328,P-331	102–103			
6-CH_3	23,505	87.5–88 5	Acetate	B.p. 168 5 (13–14)	23
	P-340	81–82	*p*-Nitrophenylhydrazone	α-form 222–227 β-form 272–274	23
	P-320	84	Semicarbazone	232–233	23
7-CH_3	266	68–69			
	140	73–78			
	274	80–81			
6-C_2H_5	P-340	84–85			
2,5-Di-CH_3	23	117			
4,6,7-Tri-CH_3	P-87	—			
2,4,6-Tri-CH_3	23	Red oil	Semicarbazone	Does not form	23
4-Iso-C_3H_7-7-CH_3	295	86			
2-C_6H_5	311,447,719,723	103–104	Benzoate ester	115–116	311,447
2-*p*-$NO_2C_6H_4$	13	192	Ethoxy	109 5	13
	427	190–195	$C_6H_5CH_2O$	α-form 143 5 β-form 144–145	13
2-*p*-$NH_2C_6H_4$	13	130			
5-OH	P-295	—			
6-OH	P-292	198			
	208	212			
6-C_6H_5CO	P-461	154–155			
5-COOH	P-441, P-442	250 (subl.)			
7-COOH	P-440	Above 300			
5-NH_2	P-349	Crystalline			
6-NH_2	P-349	165			
2-NO_2	149	104–105 (dec.)			

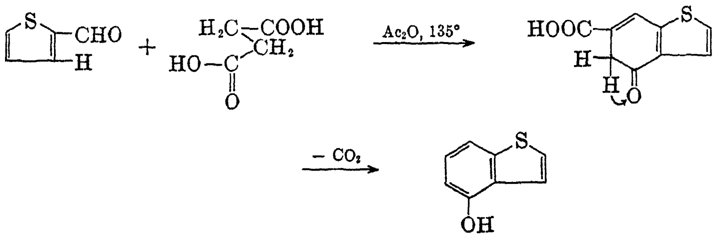
Substituents	Ref.	M.p., °C.	Hydroxyl deriv.	M.p., °C.	Ref.
5-CH_3O	P-340	102–103	3-Methoxy	72–78	208
6-CH_3O	208,P-340	119			
6-C_2H_5O	208,P-92,P-187, P-455,P-635	124–125	3-Methoxy	83	208
5-$CH_3OCH_2CH_2O$	P-247,P-574	B.p. 190 (4 mm.)			
6-$CH_3OCH_2CH_2O$	P-247,P-574	Liquid			
6-$CH_3OCH_2CH_2O$-2-COOH	P-247	81			
6-$C_2H_5OCH_2CH_2O$	P-247,P-574	84–85			
6-CH_3S	P-357	133–134			
6-C_2H_5S	P-358,P-359	84–85			
5,7-Di-CH_3O	P-193	143			
6,7-Di-CH_3O	P-249	180			
5,7-Di C_2H_5O	P-193	103			
6-F	P-571	—			
4-Cl	140	116–118			
	P-299	106			
	P-201,P-443	119–120			
5-Cl	23,P-298,P-328	100	Acetate ester	67	190,191
			2,2-Dibromo	93	P-341
7-Cl	140	103–106			
	P-443	119–120			
5-Br	416	116			
5,7-Di-Cl	P-74,P-511	140–143			
5,6,7-Tri-Cl	P-539	—			
4-CH_3-5-Cl	P-86,P-437	—			
4-CH_3-6-Cl	P-75,P-76,P-88, P-92,P-184, P-186,P-189 P-420,P-445, P-535,P-634	—			
4-CH_3-7-Cl	P-226	128–128 5			
4-CH_3-7-CN	P-446	194			

Table continued

TABLE II-12 (*continued*)

Substituents	Ref.	M.p., °C.	Hydroxyl deriv.	M.p., °C.	Ref.
5-CH_3-7-Cl	P-511	110			
5-CH_3-2,2-di-Br	P-341	99			
6-CH_3-5-Cl	P-126	125			
6-CH_3-4-Br	23	134–135	*p*-Nitrophenylhydrazone	About 200	23
6-CH_3-5-Br	P-126	125.5			
7-CH_3-5-F	P-245	104			
7-CH_3-4-Cl	P-153	—			
7-CH_3-5-Cl	P-511	106–108			
7-CH_3-6-Cl	P-72	—			
4-CH_3-5,6-diCl	P-61	—			
4-CH_3-5,7-diCl	P-257	135			
5-CH_3-4,7-diCl	P-237	160–161			
6-CH_3-4,7-diCl	P-229	145			
6-CH_3-5,7-diCl	P-511	110			
7-CH_3-4,5-diCl	P-197	173			
7-CH_3-4,6-diCl	P-229	127			
4-CH_3-5,6,7-triCl	P-539	—			
4-CH_3-5-Cl-7-OCH_3	P-191,P-19	—			
6-CH_3-4-Cl-7-COOH	P-446	Above 300			
6-CH_3-5-OCH_3-7-Cl	P-260	185–186			
4-C_2H_5-6-Cl	P-143,P-238	163			
4,5-DiCH_3-6-Cl	P-428	—			
4,5-DiCH_3-7-Cl	P-120	160			
	P-211	—			
	P-247	—			
	P-449	—			
	P-558	—			
4,6-Di-CH_3-7-Cl	P-136,P-225	111			
4,6-Di-CH_3-5-CN	P-457	174–175			
4,7-Di-CH_3-5-F	P-245	120			
4,7-Di-CH_3-6-Cl	P-250,P-634,P-535	115			

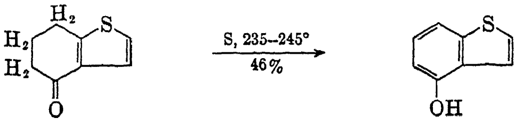
Substituents	Ref.	M.p., °C.	Hydroxyl deriv.	M.p., °C.	Ref.
5,7-Di-CH_3-4-Cl	P-136,P-225	118			
5,7-Di-CH_3-6-Cl	P-241	117–118			
4,6-Di-CH_3-5,7-diCl	P-233	224			
4,5-Di-CH_3-6-CH_3O	P-223	152–154			
4,5-Di-CH_3-6-Cl-7-CH_3O	P-223	132–133			
4,6-Di-CH_3-5-CH_3O	P-223	—			
4,6-Di-CH_3-5-C_2H_5O	P-223	—			
4,6-Di-CH_3-5-Cl-7-CH_3O	P-223	118			
4,7-Di-CH_3-6-CH_3O	P-556	150			
4,7-Di-CH_3-6-C_2H_5O	P-223,P-556	94–96			
4,7-Di-CH_3-5-CH_3O-6-Cl	P-223	129–130			
4,7-Di-CH_3-5-Cl-6-CH_3O	P-223,P-556	128–130			
4,7-Di-CH_3-5-CH_3O-6-Br	P-223	94			
6,7-Di-CH_3-5-CH_3O	P-223	150			
6,7-Di-CH_3-4-Cl-5-CH_3O	P-223	152			
4-Cl-?-CH_3O	P-524	—			
5-Cl-6-C_2H_5O	23	135 5–136.5	Acetate	128–129	23
			Semicarbazone	250	23
			p-Nitrophenylhydrazone	249–252	23
5-Cl-6-CH_3S	P-221	182–183			
5-Cl-6-C_2H_5S	P-221	136			
6-Cl-5-CH_3S	P-221	140			
4-CH_3-6-Cl-7-iso-C_3H_7	295	B.p. 191–193 (10 mm.)			
7-CH_3-5-C_6H_5CO	P-461	—			
5-(*p*-ClC_6H_4)	P-234	132–133			
4-(*p*-ClC_6H_4)-7-Cl	P-234	171			
4-(4′-Cl-5′-$CH_3C_6H_3$)-6-CH_3-7-Cl	P-234	162–163			
5-(*m*-$CH_3C_6H_4$)-4-Cl-7-CH_3	P-234	274–275			
4-CF_3-6-CH_3O	P-485	—			
5-CF_3-6-Cl	P-571	—			
7-CF_3-6-Cl	P-571	—			
2-(2′-Pyridyl)	35	132	Acetate ester	133	35
2-(2′-Quinolyl)	35	187	Acetate ester	174	35



(94)

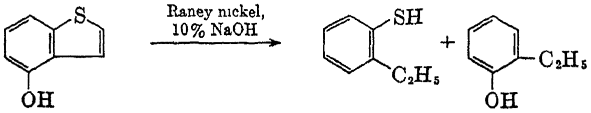
to be 4-hydroxythianaphthene (eq. 94). Biedermann reported t compound underwent the indophenine test with isatin, developed color with ferric chloride, and was converted by calcium chloride to dye. It developed an intense blue-green color with chloroform an and reacted with diazonium salts to form azo derivatives.

4-Hydroxythianaphthene has been prepared from the dehydrog of 4-oxo-4,5,6,7-tetrahydrothianaphthene (for details of prepara section III) with sulfur (184) (eq. 95). 5-Methyl-4-hydroxythiana



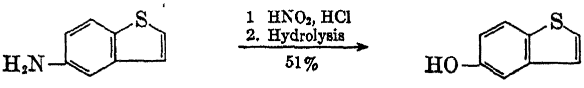
was prepared in the same fashion (318). Both of these compound coupled with diazonium salts, are substituted in the 7-position.

4-Hydroxythianaphthene, when treated with nickel-aluminu yields a mixture of *o*-ethylthiophenol and *o*-ethylphenol, indicating of the hydroxyl group or the thiol group as well as rupture of t phene ring (403) (eq. 96).



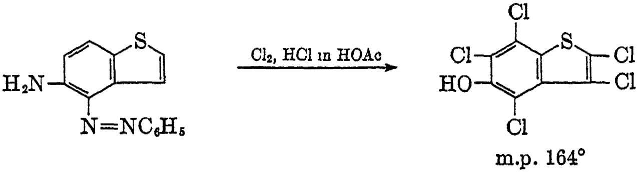
4. *5-Hydroxythianaphthenes*

5-Hydroxythianaphthene has been prepared by diazotization 5-amino derivative and hydrolysis of the diazotized product ((eq. 97). 4-Bromo-5-hydroxythianaphthene and 3,4-dibromo-5-h



thianaphthene results from the bromination of 5-aminothianaphthene (222). Nitrosation takes place in the 4-position when 5-hydroxythianaphthene is treated with zinc chloride and sodium nitrite.

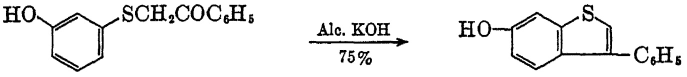
2,3,4,6,7-Pentachloro-5-hydroxythianaphthene is the end product of the chlorination of 4-phenylazo-5-aminothianaphthene (222) (eq. 98).



(98)

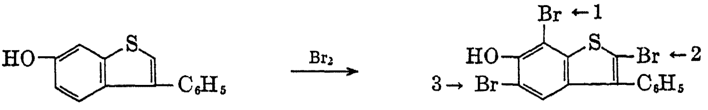
5. *6-Hydroxythianaphthenes*

The parent compound of this series is not known, but some 3-phenyl derivatives have been prepared. 3-Phenyl-6-hydroxythianaphthene has been prepared by cyclization of *m*-hydroxyphenyl phenacyl sulfide (222). (eq. 99). 6-Hydroxy-3-phenylthianaphthene forms the methyl ether with



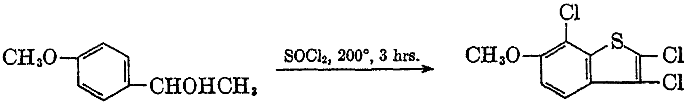
(99)

methyl sulfate. When this compound is brominated or chlorinated in a stepwise manner, the order of substitution is the 7-position, the 2-position, and finally the 5-position (eq. 100). It bears mentioning that the proof of this assignment of order was not as rigorous as is normally expected.



(100)

The methyl ether of 6-hydroxy-2,3,7-trichlorothianaphthene has been prepared from 1-(4′-methoxyphenyl)ethanol by the action of thionyl chloride (32). The mechanism of this reaction is not clear (eq. 101).



(101)

When heated for a longer period, a tetrachloro derivative, probably 6-methoxy-2,3,5,7-tetrachlorothianaphthene was obtained. It should be noted that the present authors assigned the positions of the 5- and 7-chloro atoms on the basis of the chlorination of 6-hydroxy-3-phenylthianaphthene by Fries and coworkers (222).

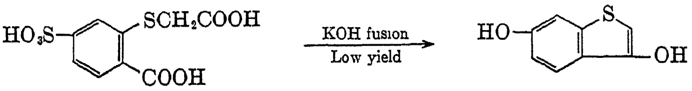
6. 7-Hydroxythianaphthene

Neither this compound nor any of its derivatives are reported in the literature. However, in certain instances dihydroxythianaphthenes with one of the hydroxyl groups in the 7-position are known and these are discussed below.

7. Di- and Trihydroxythianaphthenes

(a) **3,6-Dihydroxythianaphthene**

The preparation of this compound has been fully described by Friedländer (208) and in the patent literature (P-292). The method consists of cyclization of 2-carboxy-5-sulfophenylthioglycolic acid by fusion with potassium hydroxide. The sulfonic acid group is replaced by a hydroxyl group in the fusion step (eq. 102). This compound forms the 3,6-dimethoxy derivative when treated with dimethyl sulfate.



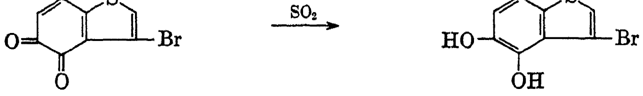
(102)

(b) **3,5-Dihydroxythianaphthene**

This compound was prepared in the same manner as its 3,6-isomer from alkali fusion of 2-carboxy-4-sulfophenylthioglycolic acid (P-295). No physical constants were given. It was stated that this compound could be converted easily to the corresponding thioindigo dye.

(c) **4,5-Dihydroxythianaphthenes**

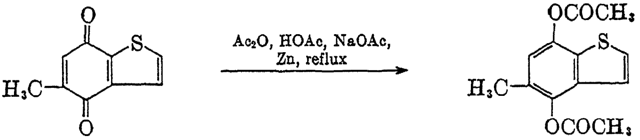
4,5-Dihydroxythianaphthene is not known, but some of its halogen derivatives have been prepared. 3-Bromo-4,5-dihydroxythianaphthen) has been formed by reduction of 3-bromo-4,5-thianaphthenequinone (222e (eq. 103). This compound reacts with acetic anhydride to form the 4,5-diacetate.



(103)

(d) 4,7-Dihydroxythianaphthenes

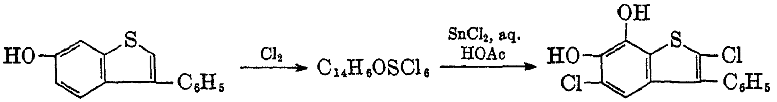
The only compound of this series reported is the diacetate of 5-methyl-4,7-dihydroxythianaphthene. This is prepared directly from the corresponding quinone by reaction with zinc and acetic acid (504) (eq. 104).



(104)

(e) 6,7-Dihydroxythianaphthenes

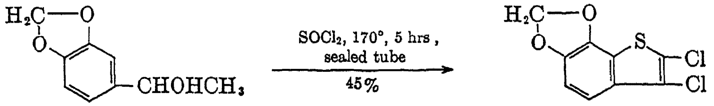
The parent compound is unknown. A compound thought to be 2,5-dichloro-6,7-dihydroxy-3-phenylthianaphthene has been prepared from 6-hydroxy-3-phenylthianaphthene as illustrated in eq. 105 (222). The



(105)

compound was not isolated and was converted to the 6,7-quinone by oxidation with nitric acid.

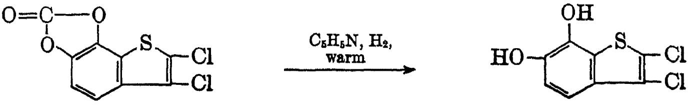
2,3-Dichloro-6,7-dihydroxythianaphthene has been synthesized through the action of thionyl chloride on 1-(3′,4′-methylenedioxyphenyl)ethanol (32) (eq. 106). α,β-Dibromo-3,4-methylenedioxystyrene, when heated



(106)

(*Note:* If original ring closure occurs in reverse fashion, the compound would be the 5,6-substituted product rather than the 6,7-isomer. The structure has not been proved.)

with thionyl chloride, also gives a 70% yield of this compound. Cleavage of the dioxolane ring was accomplished by means of pyridine in a hydrogen atmosphere (eq. 107). The compound gives a bluish-green color with

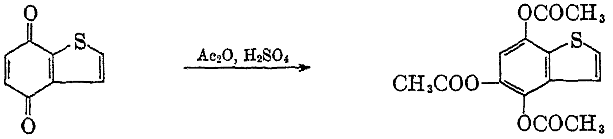


(107)

ferric chloride differing somewhat from the pure green of catechol derivatives. It is reported to form a dibenzoate derivative.

(f) Trihydroxythianaphthenes

None of these compounds are known in the free state. Only the triacetate of 4,5,7-trihydroxythianaphthene (m.p. 151–153°) is reported in the literature (184). It is formed by treating 4,7-thianaphthenequinone



(108)

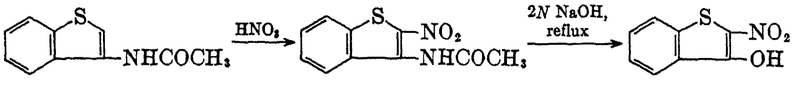
with acetic anhydride in sulfuric acid (eq. 108). This compound was saponified and oxidized by means of ferric chloride to 5-hydroxy-4,7-thianaphthenequinone.

C. Reactions of Hydroxythianaphthenes

1. *Reactions of the Enol Form*

Some of the main reactions of the enol form of 3-hydroxythianaphthenes are presented in the sections on hydroxythianaphthenecarboxaldehydes and thianaphthene 1-dioxides. Their reduction to thianaphthenes was discussed in section I.

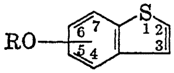
Attempts to substitute the hydroxythianaphthenes with such reagents as nitric acid or sulfuric acid cause rearrangement and oxidation of the keto form, and the thioindigo dyes result. This is discussed in considerable detail in Chapter III. The only oxidation of these materials that does not yield the thioindigo dyes is carried out with hydrogen peroxide. This oxidation produces the 1-dioxides (sulfones). (See section XIV). While 3-hydroxy-2-thianaphthenesulfonic acid is not reported, 2-nitro-3-hydroxythianaphthene has been prepared by a circuitous method involving 3-acetamidothianaphthene (149) (eq. 109). This orange-colored compound gives a wine red color with ferric chloride solution.



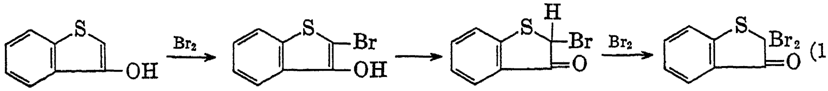
(109)

When 3-hydroxythianaphthene is treated with chlorine or bromine a 2-halo derivative is formed. This compound apparently exists in the keto form, since a second halogen also enters the 2-position to form the 2,2-

TABLE II-13. Derivatives of Benzenoid Hydroxythianaphthenes

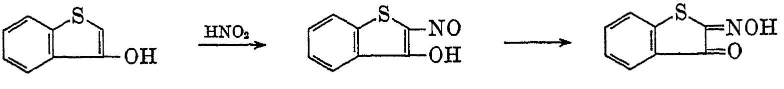


Position of hydroxyls or hydroxyl derivs.				
Position	R	Other substituents	M p., °C.	Ref.
5-	H	3-Br	137.5–138	747
5-	H	4-Br	112	222
			108–109	747
5-	H	3,X-DiBr	146–148	747
5-	H	3,4-DiBr	103	222
5-	H	4,X-DiBr	93–94	747
5-	H	3-NO_2-4-Br	173 (dec.)	222
5-	H	2,3,4,6,7-PentaCl	164	222
5-	CH_3	4,7-Dioxo	205–206	184
5-	H	4-Oxo-7-anil-3-Br	213 (dec.)	222
5-	CH_3CO	3-Br	100.5–101	747
5-	$CH_2{=}CHCH_2$	None	Oil	747
5-	H	4-$CH_2{=}CHCH_2$	B.p. 145–150 (2 mm.)	747
			α-Naphthylurethan, m.p. 166–168	747
5-	H	4,6-$(CH_2{=}CHCH_2)_2$	B.p. 155–160 (2 mm.)	747
			α-Naphthylurethan, m.p. 152–154	747
6-	H	5-CH_3	146–147	763
6-	CH_3	5-CH_3	62–63	763
6-	CH_3	5-CH_3, picrate	107–108	763
6-	H	3-C_6H_5	81	222
6-	H	3-C_6H_5-7-Br	102	222
6-	H	3-C_6H_5-2,7-di-Cl	99	222
6-	H	3-C_6H_5-2,7-di-Br	128	222
6-	H	3-C_6H_5-2,5,7-tri-Cl	113	222
6-	H	3-C_6H_5-2,5,7-tri-Br	164	222
6-	H	3-C_6H_5-hexa-Cl	167 (dec.)	222
6-	CH_3	3-C_6H_5	59	222
6-	CH_3	3-C_6H_5-7-Br	113	222
6-	CH_3	3-C_6H_5-2,7-Di-Br	177	222
6-	CH_3	2,3,7-Tri-Cl	153	32
6-	CH_3	2,3,5,7-Tetra-Cl	109–111	32
4,5-	H	3-Br	248	222
4,5-	CH_3CO	3-Br	140	222
4,7-	CH_3CO	5-CH_3	116–117	504
6,7-	H	2,3-Di-Cl-	148	32
6,7-	C_6H_5CO	2,3-Di-Cl-	185	32
6,7-	H	3-Phenyl-2,5-di-Cl	160	222
6,7-	CH_3CO	3-Phenyl-2,5-di-Cl	152	222
4,5,7-	CH_3CO	None	151–153	184



(110)

dihalo derivative (46,201,P-314) (eq. 110). A somewhat similar transformation takes place when 3-hydroxythianaphthene is treated with nitrous acid. The 2-nitroso derivative quickly rearranges to the 2-oxime of the keto form (P-5,P-315) (eq. 111). The same compound results from the



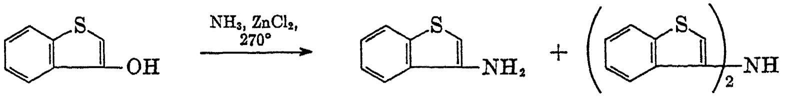
(111)

action of nitrous acid on 3-hydroxy-2-thianaphthenecarboxylic acid (46). It is well established that 2-groups are readily replaced in oxidation reactions. Ordinarily, when the reaction is carried out with stronger oxidizing agents, oxidative cleavage of such substituents occurs and thioindigo dyes result.

3-Hydroxythianaphthene couples with diazonium salts at the 2-position. Friedländer (202) first discovered this reaction in 1910 when he noted that benzenediazonium chloride or its *p*-nitro derivative coupled to give orange-red dyes. A Swedish patent (P-662) describes a chemotherapeutic compound obtained by coupling 6-methyl-3-hydroxythianaphthene with diazotized sulfanilamide. Dyes in which the 2-azophenyl substituent is substituted with a sulfo group, or with methyl and chloro groups, have been described (P-83). Benzidine, when diazotized, couples with two molecules of 3-hydroxythianaphthene in the 2-position (428).

Reactions typical of a phenolic hydroxyl group are demonstrated by the ability of 3-hydroxythianaphthene to form the methoxy ether with dimethyl sulfate (197,20) (later investigators could not accomplish this (675)), methyl iodide in the presence of alkali (20,14,22), or diazomethane (675). When 3-hydroxythianaphthene is boiled with acetyl chloride or acetic anhydride, the acetate is formed (23). The sodium salt of 3-hydroxythianaphthene yields the carbonate when treated with phosgene (P-371). Tetraacetylbromoglucose reacts with 3-hydroxythianaphthene (131). Hydrolysis with barium hydroxide, or, better, with alcoholic ammonia, yields "thioindican" (3-thianaphthenyloxy glucoside, m.p. 73.5°).

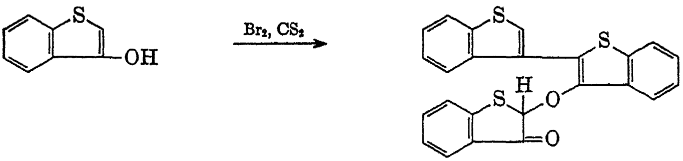
The hydroxyl group of 3-hydroxythianaphthene, when treated with ammonia in the presence of zinc chloride or calcium chloride, is replaced with the amino group. The 3-aminothianaphthene appears to react further with another mole of 3-hydroxythianaphthene to yield the secondary amine di-(3-thianaphthenyl)amine (324). Apparently, this second reaction proceeds with considerably more ease than the first, and 3-aminothianaphthene is the minor product of the reaction (eq. 112). The re-



(112)

action also can be carried out with ammonium sulfite at 100° or with dilute ammonia alone at 180°. Even acetamide, when heated with 3-hydroxythianaphthene, yields the secondary amine. 3-Acetamidothianaphthene was isolated in 30% yield when short reaction periods were employed.

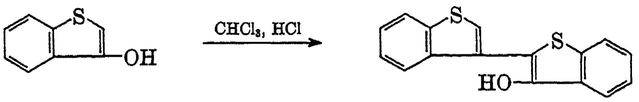
3-Hydroxythianaphthene undergoes a complex condensation when brominated in carbon bisulfide solution (334) (eq. 113). The keto form of



(113)

m.p. 198–199°

this compound is indicated by its inability to form a methoxy ether with dimethyl sulfate. 2-Bromo-3-hydroxythianaphthene also decomposes to yield this compound. In a chloroform solution containing hydrogen chloride, a dehydration reaction takes place which appears to be the first step of the above reaction (eq. 114). The methoxy derivative of this com-

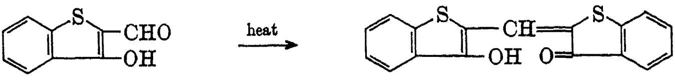


(114)

m.p. 132–133°

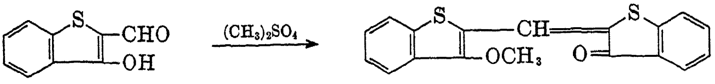
pound, prepared by the action of dimethyl sulfate, melts at 96–97°.

A rather peculiar reaction of 3-hydroxy-2-thianaphthenecarboxaldehyde involves a condensation which eliminates one of the carboxaldehyde groups (204,P-138,216,452,497) (eq. 115). Apparently, carbon monoxide and



(115)

water are eliminated in this reaction. An attempt to methylate 3-hydroxy-2-thianaphthenecarboxaldehyde with dimethyl sulfate gives 2-(3′-methoxy-



(116)

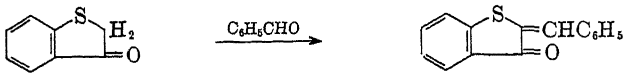
2-thianaphthenylidene)-3-thianaphthenone (eq. 116). This compound is an orange-colored solid melting at 218–220°.

2. Reactions of the Keto Form

The existence of the keto form of the hydroxythianaphthenes is easily established by means of the reactions with typical ketone reagents such as semicarbazide and phenylhydrazine. These derivatives with corresponding references are recorded in Table II-11.

The reactions of this form involving mild oxidation are very important, since thioindigo dyes are produced directly. Chapter III is devoted almost entirely to these dyes and to reactions of this form with compounds capable of producing chromophoric groups in the resultant condensation product.

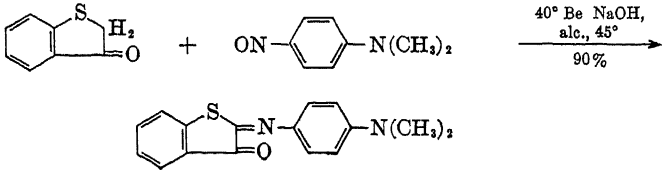
Aromatic aldehydes condense with the active hydrogens in the 2-position of the keto form and arylidene-type derivatives result (eq. 117).



(117)

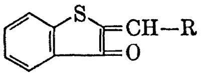
Auwers and Arndt (18) found that the 5-methyl-2-benzylidene derivative added one mole of bromine at the double bond to give a dibromide, m.p. 116°. The 2-benzylidenes are mild dyes and are discussed in more detail in Chapter III. However, their melting points and some of their colors are listed in Table II-14. While the yields of the benzylidene derivatives are not generally reported in the literature, they would appear to be quite high, since it is reported that the condensation of the keto form of 3-hydroxythianaphthene with 2-anthraquinone aldehyde can be used for the estimation of thioindoxyl (365).

Aromatic nitroso compounds condense with the active keto form to produce anils (eq. 118). Here again a chromophoric group is produced and brilliantly colored crystalline derivatives are formed. These compounds have been evaluated as dyes but their stability did not warrant commercial



(118)

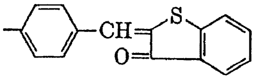
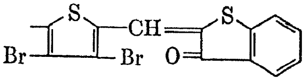
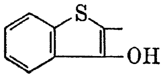
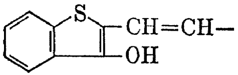
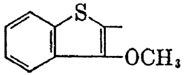
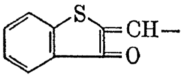
TABLE II-14. 2-Benzylidene Derivatives of 3-Thianaphthenone and Its Derivatives



Substituents	R	M.p., °C.	Color	Ref.
None	C_6H_5	127	Yellow	106,202
		132	Yellow	262
		200	—	256
	m-HOC_6H_4	212	Lemon-yellow	202
		252	—	256
	p-HOC_6H_4	262	Orange-yellow	202
	o-$NO_2C_6H_4$	171	Orange-red	398,202
	p-$NO_2C_6H_4$	231	Orange	202
		264	—	256
		273	—	262
	m-$NO_2C_6H_4$	233	—	256
	m-$NH_2C_6H_4$	157	Brown-yellow	256
	p-$(CH_3)_2NC_6H_4$	202	Red	256,262
	p-ClC_6H_4	118	—	256
	p-$CH_3C_6H_4$	159	—	256
	3,4-$C_6H_3(OH)_2$	231	—	256
		280	Brown-orange-yellow	202
	Piperonylidene (for $=CHR$)	207	Bright yellow	202
		248	—	256
	3-CH_3O-4-$CH_3C_6H_3$	194	—	256
	$C_6H_5CH=CH$	184	—	256
	C_6H_5NH	160	Brown	315
	2-Anthraquinonyl	320	Bright yellow	365
		334–336	Tan	432

Table continued

TABLE II-14 (*continued*)

Substituents	R	M.p., °C.	Color	Ref.
None.		192–193	Yellow	292
		No m.p.	Copper-red	483
		270–271	Red	452,497
		255–257	Bronze	497
		218–220	Orange	334
		303	Dark red	262,183,207,403
	$(ClCH_2CH_2)_2NC_6H_4$—	191 214	Red Orange	8 P-145
	$=C(COCH_3)_2$ (for $=CHR$)	142–143	Reddish-yellow	290

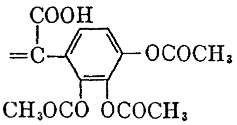
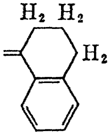
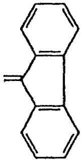
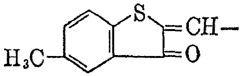
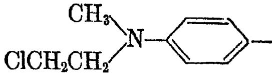
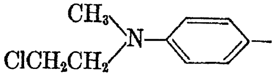
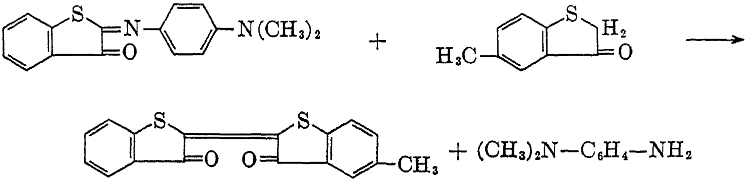
Substituents	R	M.p., °C.	Color	Ref.
None		—	Yellowish-red	186
	 (for =CHR)	250 (dec.)	Red-violet	292
	 (for =CHR)	200–202	Red	202
4-CH_3	C_6H_5	191	Yellow	262
	p-$NO_2C_6H_4$	273	Yellow-orange	262
	p-$(CH_3)_2NC_6H_4$	202	Greenish-orange	262
5-CH_3	C_6H_5	147	Yellow	18,256
	p-$CH_3C_6H_4$	159	Yellow	256
	p-ClC_6H_4	178	Bright yellow	256
	p-$(CH_3)_2NC_6H_4$	198–199	Red	256
	p-$NO_2C_6H_4$	264	Orange-red	256
	m-$NO_2C_6H_4$	233	Yellow	256
	p-HOC_6H_4	252	Light brown	256
	m-HOC_6H_4	200	Deep yellow	256

Table continued

TABLE II-14 (*continued*)

Substituents	R	M.p., °C.	Color	Ref.
5-CH_3	p-$CH_3OC_6H_4$	157	Bright yellow	256
	3,4-$(HO)_2C_6H_3$	248	Light brown	256
	3-CH_3O-4-HOC_6H_3	194	Deep yellow	256
	Piperonylidene (for =CHR)	231	Deep yellow	256
	$C_6H_5CH{=}CH$	184	Orange yellow	256
		>300	Red	256
6-CH_3	C_6H_5	134–135	Yellow	260
	p-$(CH_3)_2NC_6H_4$	193	Greenish-yellow	260
	p-$NO_2C_6H_4$	228–229	Yellowish-orange	260
7-CH_3	C_6H_5	130	Tan	270
	p-$(CH_3)_2NC_6H_4$	150	Greenish-yellow	270
	p-$NO_2C_6H_4$	247	Yellow-orange	270
6-C_2H_5O		152	Red	8
6-Cl		191	Red	8
	3-Benzylidenes (*from 2-Hydroxythianaphthene*)			
None	p-$(CH_3)_2NC_6H_4$	164–165	Steel-blue	370
	p-$CH_3OC_6H_4$	96–98	—	371

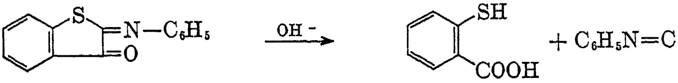
development. They are the most commonly used intermediate in the production of the unsymmetrical as well as the symmetrical thioindigo dyes because they condense with a molecule of thioindoxyl to eliminate the anil



(119)

portion of the molecule as an amine (eq. 119). This synthesis assures the formation of thioindigo dyes free of thioindirubins.

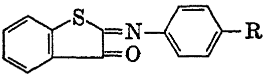
Caustic is reported to cleave the 2-phenyl anil of 3-thioindoxyl and phenyl isocyanide (carbylamine) results (91) (eq. 120). This reaction is



(120)

reminiscent of the preparation of 3-hydroxy-2-thianaphthenecarboxaldehyde from the action of caustic on the thianaphtheneindole indigos (see section IX-a). Anils of this class which have been isolated and characterized are listed in Table II-15 along with references, melting points, and colors. Since these materials have enjoyed wide use as dye intermediates, reference has been made, particularly in the patent literature, to a very large number that have not been properly characterized. Thus, the greater proportion of these anils have not been mentioned in the table, since it is difficult in patent literature to differentiate between the authentic and the fictitious.

TABLE II-15. 2-Anils of 2,3-Thianaphthenequinone and Its Derivatives



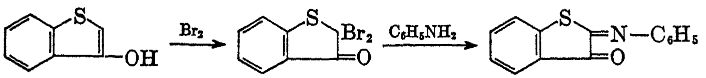
Substituents	R	M.p., °C.	Color	Ref.
None....................	H	151–152	Orange	46, 417
	CH_3	159	—	46
	OH	210	—	P-581
		251–252	Brown	378,282
	NHC_2H_5	158	Carmine-red	P-320
	NHC_6H_5	193	Green	417
	$N(CH_3)_2$	176	Green-red	417,P-320
	p-NH_2—C_6H_4	193	—	P-320

Table continued

TABLE II-15 (*continued*)

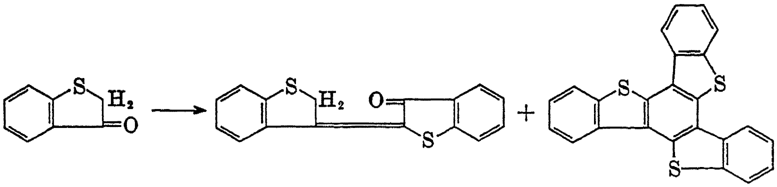
Substituents	R	M.p., °C.	Color	Ref.
4-CH_3	OH	234–236	—	140
5-CH_3	OH	—	—	140
	$N(CH_3)_2$	200	Green	417
7-CH_3	OH	248–250	—	140
6-C_2H_5O	H	118–119	Yellow	211
	OCH_3	141	—	P-581
	OH	237–239	—	282
	$N(CH_3)_2$	157	Green	378
5-$CH_3OCH_2CH_2O$	$N(CH_3)_2$	130	—	P-247
6-$C_2H_5OCH_2CH_2O$	$N(CH_3)_2$	121	—	P-247
4-Cl	OH	—	—	140
	$N(CH_3)_2$	211–212	—	140
5-Cl	$N(CH_3)_2$	148–149	—	417
6-Cl	$N(CH_3)_2$	190	—	212
7-Cl	OH	272–273	—	140
	$N(CH_3)_2$	147	—	417
4-CH_3-7-Cl	$N(CH_3)_2$	206–207	—	P-226
6-CH_3-5-Cl	$N(CH_3)_2$	226–227	—	P-126
7-CH_3-5-Cl	$N(CH_3)_2$	206	Green	378
4-C_2H_5-6-Cl	H	—	Yellowish-rose	P-238
6-CH_3S-5-Cl	$N(CH_3)_2$	230–231	—	P-221
6-C_2H_5S-5-Cl	$N(CH_3)_2$	192–193	—	P-221
4,6-Di-CH_3-7-Cl	$N(CH_3)_2$	255	—	P-136,P-225
5,7-Di-CH_3-4-Cl	$N(CH_3)_2$	253	—	P-136
4-C_6H_4-4′,7-di-Cl	$N(CH_3)_2$	332	—	P-234
4-C_6H_3-4′,7-di-Cl-5′,6-Di-CH_3	$N(CH_3)_2$	241–242	—	P-234

Another method of forming the anils consists of brominating the 3-hydroxythianaphthene and subsequently reacting the 2,2-dibromo derivative of the keto form with an aromatic amine (46) (eq. 121). This route has been used frequently in the production of thioindigo dyes.



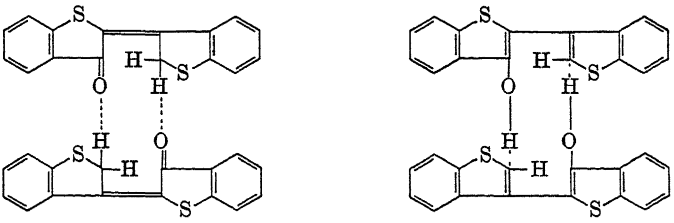
(121)

3-Hydroxythianaphthene, heated to boiling in dichloroacetic acid solution, undergoes a self condensation to give a dimeric condensate (3-oxo-2,3′-bithianaphthene) and trimeric condensate (benzo[1,2-*b*, 3,4-*b*′, 5-6-*b*″]-tristhianaphthene) II (140a). Compound I, which can be converted to II by reaction with another mole of thioindoxyl, was found to exist as a "bimolecular associate." Since compound I is planar, the investigators



(122)

(I, m.p. 225–226°) (II, m.p. 422–425°)



(IA) (IB)

(123)

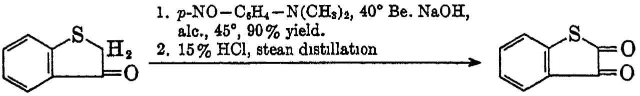
felt that this association might readily occur through hydrogen bonding, the product being further stabilized as a resonance hybrid of the forms IA and IB (eq. 123).

VII. Thianaphthenequinones

A. 2,3-Thianaphthenequinones

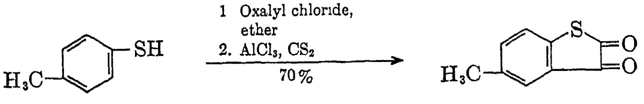
This class of compounds can be prepared from the 3-hydroxythianaphthenes, or by forming the thiophene ring through reaction of thiophenols with oxalyl chloride. These compounds are normally reddish materials with relatively poor dyeing properties. However, they are used as intermediates in the synthesis of thioindigos, thioindirubins, thioindogenides, etc., and will be discussed in greater detail in Chapter III.

2,3-Thianaphthenequinones can be prepared from 3-hydroxythianaphthenes by converting these materials to their 2-anils or 2-oximes, followed by a simple hydrolysis with acid (P-5,P-315,P-320,417,378,P-226,P-234). Perhaps the most complete laboratory details are given by Pummerer (417) (eq. 124).


S
H₂
O
1. p-NO–C_6H_4–N$(CH_3)_2$, 40° Be. NaOH, alc., 45°, 90% yield.
2. 15% HCl, stean distillation
S
O
O

(124)

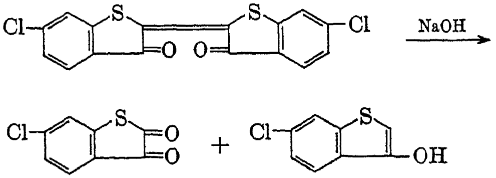
Probably the most convenient synthesis involves a ring closure reaction of thiophenol and oxalyl chloride. The two-step reaction was first noted by Stollé (490). Later investigators give detailed procedures and claim better yields (403). The reaction is demonstrated with *p*-thiocresol (eq. 125). This method has been reported frequently in the patent litera-



(125)

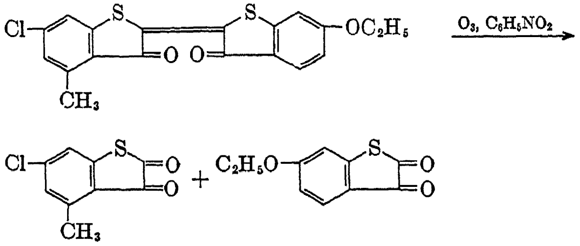
ture for the preparation of derivatives of thianaphthenequinones (P-461) and for the preparation of naphthothiophenequinones (see Chapter V).

Other less practical methods require cleavage of thioindigo dyes with caustic (212). The reaction is demonstrated with 6,6′-dichlorothioindigo (eq. 126).



(126)

An oxidative cleavage with ozone of 6-chloro-4-methyl-6′-ethoxythioindigo suspended in nitrobenzene, gives the quinone of each of the two parts of the thioindigo dye (eq. 127). This is not a very practical method,



(127)

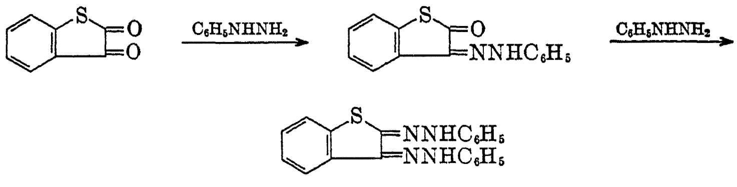
since fractional recrystallization is required to separate the two products, but it may be applied to symmetrical thioindigo dyes with fair results.

Only a few of the many thianaphthenequinones that have been reported have actually been isolated and characterized. The melting points of the isolated compounds are listed in Table II-16.

Recent investigators (282,140,140a,141) have studied the comparative reactivities of the carbonyl groups in the substituted 2,3-thianaphthenequinones. By close examination of a series of nearly 100 dyes prepared from the thianaphthenequinones and 3-thioindoxyls (3-hydroxythianaphthenes) it was concluded that unsubstituted 2,3-thianaphthenequinone nearly always gave both 2-oxo and 3-oxo condensation, *i.e.*, both thioindigo and thioindirubin dyes were formed in the condensation with thioindoxyls. A substituent in the 4-position in the thianaphthenequinone almost always caused condensation through the 2-keto group (due to steric hindrance). A substituent in the 5-position of the quinone also usually caused condensation through the 2-oxo group alone. A substituent in the 6-position usually gave condensation products resulting from both the 2-oxo and 3-oxo groups. A substituent in the 7-position of the quinone is without apparent effect. In the absence of other substituents in the quinone, substituents in the thioindoxyl molecule determine the type of condensation. These are apparently the only conditions in which the thioindoxyl molecule exerts a dominant influence. A fused benzene ring in the 4,5- and 6,7-positions usually causes condensation to take place through the 2-oxo group. The benzene ring fused to the 5,6-positions always gives rise to a mixture of products resulting from condensations of both carbonyl groups.

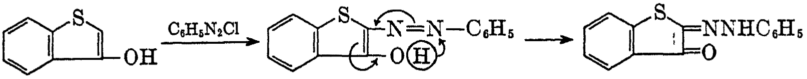
In the past it had been accepted that 2,3-thianaphthenequinones condensed through the 3-keto group, but in view of the work by the above investigators, the reactions of these quinones with reagents other than thioindoxyls should be reinvestigated. In view of the lack of further work on this subject, the condensation reactions listed below are assumed to take place at the 3-position in preference to the 2-position.

2,3-Thianaphthenequinone, when reacted with amines or typical ketone reagents, such as the hydrazines, yields 3-substitution products as the first step of the reaction. Subsequent reaction with excess reagent yields the 2,3-disubstitution products (eq. 128). The isomeric 2-phenylhydrazone



(128)

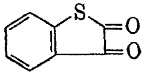
has been prepared from 3-hydroxythianaphthene by diazotization (19). The investigators indicated that the corresponding diazo derivative rearranged to the hydrazone (eq. 129). When treated with one mole of



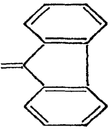
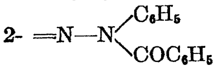
(129)

phenylhydrazone this compound gives the same osazone obtained from 2,3-thianaphthenequinone and excess phenylhydrazine.

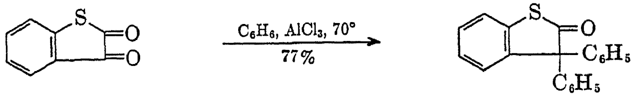
TABLE II-16. Physical Constants of 2,3-Thianaphthenequinones and Their Derivatives



Substituents	Ref.	M.p., °C.	Deriv.	M.p., °C.	Ref.
None....................	183 207	116 121	2-Oxime	172 (dec.)	46,P-5,P-315
			2- $=N{-}OCH_3$	125	46
			2- $=NOOCCH_3$	174	46
			2- $=NOSO_2C_6H_5$	231	46
			2- $=NOOCC_6H_5$	170	19
			3-Oxime	181 (dec.)	371,46
				186	46
			2-Phenylhydrazone	194	19
			3-Phenylhydrazone	164–165	149,19
				166–167	46
			2,3-Diphenylhydrazone	199–200	19
			2- $=N{-}N\begin{smallmatrix}C_6H_5\\CH_3\end{smallmatrix}$	133–134	19
			2- $=N{-}N\begin{smallmatrix}C_6H_5\\COC_6H_5\end{smallmatrix}$	α-form 141 β-form 156	19
			3- $=N{-}N\begin{smallmatrix}C_6H_5\\CH_3\end{smallmatrix}$	98–99	19
				122–123	26
			3- $=N{-}N\begin{smallmatrix}C_6H_5\\COC_6H_5\end{smallmatrix}$	199	19
			3- $=N{-}N{=}C(C_6H_5)_2$	107–108 5	229

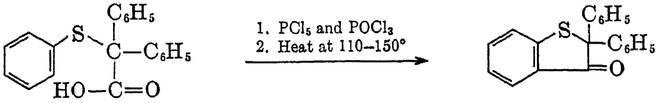
Substituents	Ref.	M.p., °C.	Deriv.	M.p., °C.	Ref.
			3- =N—N= 	221–223	229
4-CH$_3$	140	120–121			
5-CH$_3$	P-320,417	143–144	2-Oxime	188	19
	140,490	144–145	2-Phenylhydrazone	186 5	19
	403	146–147	 $2\text{- }{=}N{-}N(C_6H_5)(COC_6H_5)$	α-form-145 β-form-157	19
6-CH$_3$	Not reported	—	2-Oxime	178	P-340
7-CH$_3$	140	126–127	—		
6-C$_2$H$_5$	Not reported	—	2-Oxime	176	P-340
6-CH$_3$O	Not reported	—	2-Oxime	208–209 (dec.)	P-359
6-C$_2$H$_5$O	225	160			
	378	162	3-Phenylhydrazone	142	378
6-CH$_3$S	Not reported	—	2-Oxime	178	P-358
4-Cl	140	138–139			
6-Cl	212	134			
7-Cl	140	149–150			
4-CH$_3$-6-Cl	378,225	129–130	3-Phenylhydrazone	169	378
	212	132			
4-CH$_3$-7-Cl	P-226	158			
6-CH$_3$-5-Cl	P-126	188			
7-CH$_3$-5-Cl	378	135	3-Phenylhydrazone	183	378
4-C$_2$H$_5$-6-Cl	P-238	—			
4-C$_6$H$_5$-4,7-di-Cl	P-234	239–240			
5-C$_6$H$_5$-4-Cl	P-234	213–214			
7-CH$_3$-5-C$_6$H$_5$CO	P-461	—			
6-CH$_3$S-5-Cl	P-221	213			
6-C$_2$H$_5$S-5-Cl	P-221	160–161			

Further activity of the 3-oxo group can be demonstrated by the ability of 2,3-thianaphthenequinone to react as a typical *o*-quinone with aromatic compounds in the presence of aluminum chloride (519). Thus, with benzene, 2,3-dihydro 3,3-diphenyl-2-thianaphthenone is obtained (eq. 130).



(130)

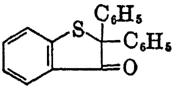
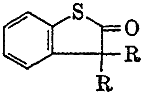
2,3-Dihydro 3,3-di-*p*-tolyl-2-thianaphthenone was prepared in the same manner. Another catalyst is sulfuric acid, which can be employed with phenols, thiophenol, or dimethylaniline (142). Potassium bisulfate acts as a catalyst in the condensation of thiophenol, α-naphthol, and dimethylaniline (142). The investigators report that 2,3-dihydro-3,3-di-(*p*-hydroxyphenyl)-2-thianaphthenone is converted to a "diphenylthianaphthenequinone-red," m.p. 219°, upon oxidation with potassium ferricyanide. This can be reduced with zinc and acetic acid to "leucodiphenylthianaphthenequinone-red," m.p. 192–193°.



(131)

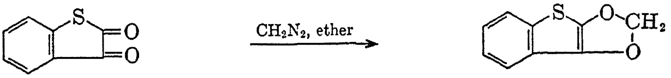
The isomeric 2,3-dihydro-2,2-diphenyl-3-thianaphthenone is prepared in quite another manner through ring closure of diphenylphenylthioglycolic acid (51) (eq. 131).

TABLE II-17. Diaryl Derivatives of 2,3-Dihydrothianaphthenone

Compound	M.p., °C.	Ref.
	150	51
		
R = C_6H_5	128	519
R = *p*-$CH_3C_6H_4$	140–141	519
R = *p*-HOC_6H_4	235–236	142
R = *p*-HSC_6H_4	59–60	142
R = *p*-$(CH_3)_2NC_6H_4$	184.5	142
R = *o*-α-$HOC_{10}H_6$	86	142

The melting points of these compounds are tabulated in Table II-17.

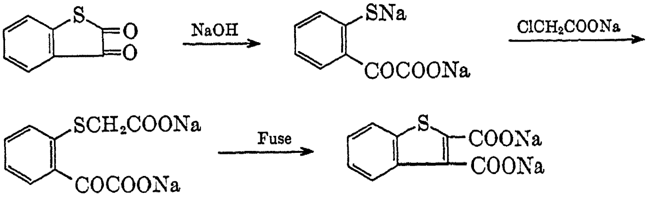
When 2,3-thianaphthenequinone is treated with diazomethane, thianaphtheno[2,3-*b*][1,3]dioxole (m.p. 130°) results (446) (eq. 132). The



(132)

original quinone is obtained by hydrolysis or oxidation of the product with air. Coumarandione and naphthofurandione both undergo similar reactions.

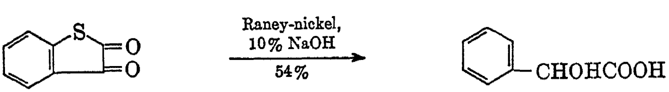
The thiophene ring of 2,3-thianaphthenequinone is easily cleaved by caustic. The resultant *o*-mercaptophenylglyoxylic acid is extremely useful in the synthesis of 2,3-thianaphthenedicarboxylic acids (46,378). These reactions are illustrated by eq. 133. This synthesis has also been widely



(133)

employed in preparing 2,3-dihydro-2-oxo-3-thianaphthenecarboxylic acid (see below).

As in the case of 4-hydroxythianaphthene described above, Raney nickel alloy ruptures the thiophene ring of 2,3-thianaphthenequinones and mandelic acids result (403) (eq. 134). *m*-Methylmandelic acid results in

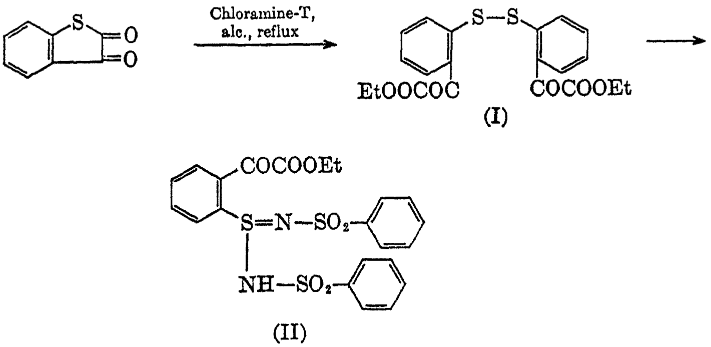


(134)

80% yield when 5-methyl-2,3-thianaphthenequinone is reduced in the same manner.

Chloramine-T reacts with 2,3-thianaphthenequinone in boiling alcohol to yield II (140b). The investigators established that the reaction proceeded through the intermediate 2,2′-dicarbethoxyketophenyl disulfide (I); the conversion from the disulfide to the final product is an application of the Alexander and McCombie reaction (eq. 135). This reaction was found to be general for the substituted 2,3-thianaphthenequinones.

2,3-Thianaphthenequinone reacts with such materials as *o*-phenylenediamine or dicyandiamide to give a fused pyrazine ring adjacent to the thiophene ring. For references and further details see Chapter VIII.



(135)

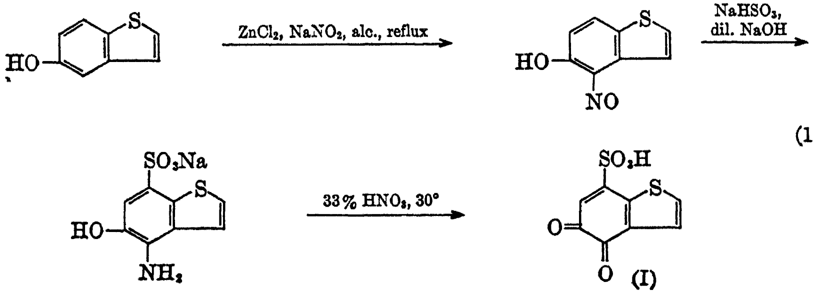
The toxicity of the thianaphthenequinones is not reported. One investigation (641) reports that 2,3-thianaphthenequinone produces a serious injury to the cornea of rabbits.

B. Benzenoid Thianaphthenequinones

The compounds of this class are quite difficult to synthesize and, at best, the overall yields are discouraging. However, their relationship to certain compounds of the naphthoquinone series having vitamin K activity has led to the synthesis of several isomeric 4,7-thianaphthenequinone derivatives. Feiser and coworkers (183,184) have studied compounds of this series in relationship to the naphthoquinones. They found that quinones having a thiophene ring in place of a benzene ring of *ortho*- and *para*-naphthoquinones are about 75 mv. higher in reduction potential than the naphthoquinones of corresponding structure. This, they concluded, indicates a lower degree of aromaticity for thiophene as compared with benzene.

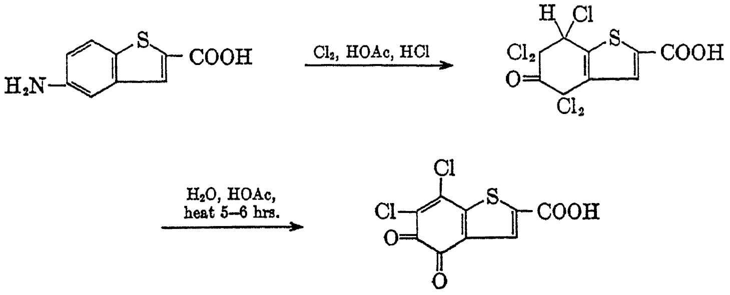
1. 4,5-Thianaphthenequinones

The parent compound is not known. However, its 7-sulfo derivative has been synthesized from 5-hydroxythianaphthene (eq. 136) (184).



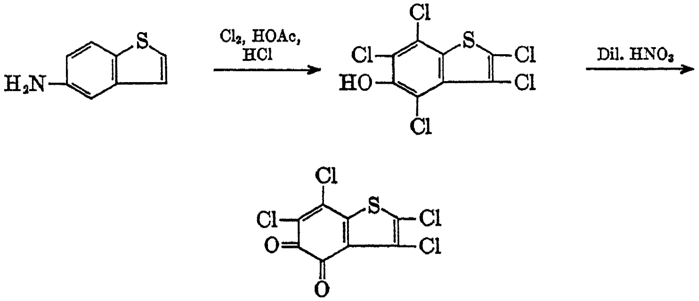
(136)

Fries and coworkers (222) prepared 6,7-dichloro-2-carboxy-4,5 thianaphthenequinone from 5-amino-2-thianaphthenecarboxylic acid by the series of reactions of eq. 137. Compound II could also be prepared by oxidation of 5-hydroxy-4,6,7-trichloro-2-thianaphthenecarboxylic acid with nitric acid in acetic acid solution. In addition, these investigators prepared 2,3,6,7-tetrachloro-4,5-thianaphthenequinone from 5-aminothianaphthene by a similar route (eq. 138). Compound III, when heated with aniline, does not form an anil. Instead, the 7-chloroatom is replaced by aniline (eq. 139). Strangely enough, compound II forms a dianil which would indicate that the 7-chloro atom is deactivated by the 2-carboxy group.



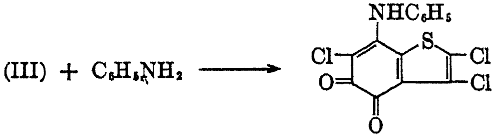
(II)

(137)



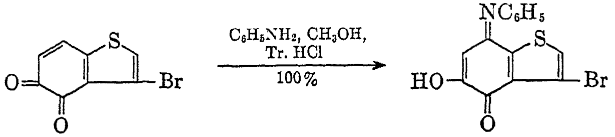
(III)

(138)



(139)

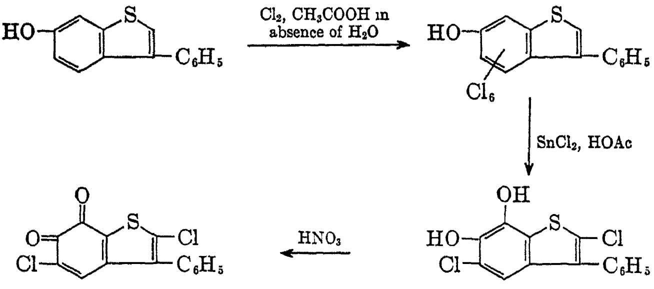
A deep violet colored 3-bromo-4,5-thianaphthenequinone has been prepared by direct oxidation of 3,4-dibromo-5-hydroxythianaphthene with nitric acid in chloroform. In contrast to other quinones of this series, this compound is reported to sublime and decompose at the relatively low temperature of 130°. This compound undergoes an interesting 1,4-addition when treated with aniline and a deep copper colored compound, 3-bromo-7-anil-5-hydroxy-4-thianaphthenone, is obtained (eq. 140).



(140)

2. *6,7-Thianaphthenequinones*

6,7-Thianaphthenequinone has not been reported. Fries and coworkers (222) have synthesized a red quinone indicated to be 2,5-dichloro-3-phenyl-6,7-thianaphthenequinone from 6-hydroxy-3-phenylthianaphthene. The synthesis involved is similar to that reported above by the same investigators for chloro derivatives of the isomeric 4,5-quinone (eq. 141). The reaction of aniline with IV was not reported.

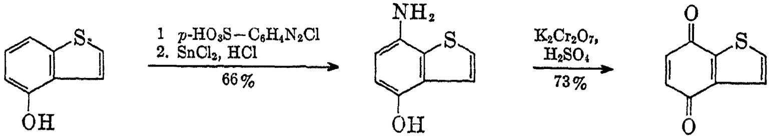


(IV)

(141)

3. *4,7-Thianaphthenequinones*

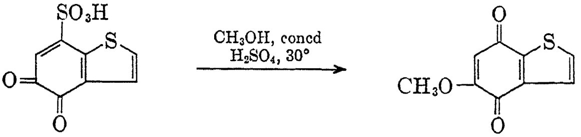
4,7-Thianaphthenequinone, a yellow crystalline substance, has been prepared from 4-hydroxythianaphthene by introduction of a 7-amino group followed by oxidation (184) (eq. 142). The compound is easily volatilized



(142)

and has an odor resembling *p*-benzoquinone.

7-Sulfo-4,5-thianaphthenequinone (I) is converted to 5-methoxy-4,7-thianaphthenequinone by a 1,4-addition of methanol (eq. 143). This

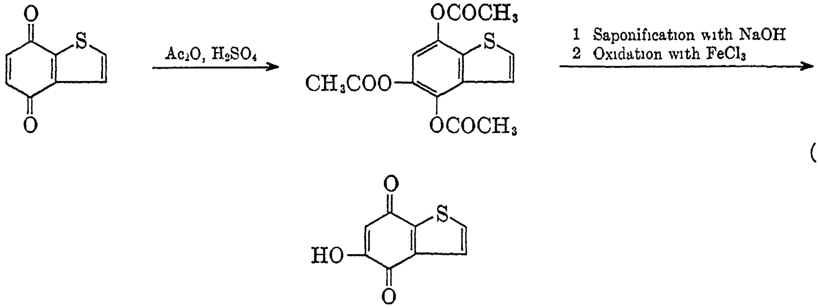


(V)

(143)

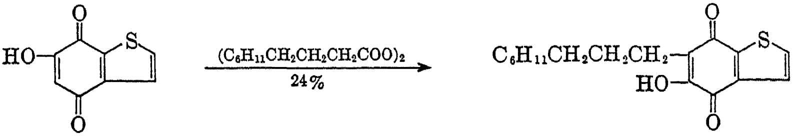
reaction further illustrates that the thiophene ring has no practical influence on the resonance of the quinone ring structure, since this is a reaction typical of benzoquinones. Normally, the thiophene ring is so highly active that its sulfonation might have been expected.

A somewhat similar reaction which yields the 5-hydroxy derivative of V further demonstrates the high reactivity of the benzenoid ring of these quinones. When acetic anhydride reacts with 4,7-thianaphthenequinone in concentrated sulfuric acid, 4,5,7-triacetoxythianaphthene results. This is converted to 5-hydroxy-4,7-thianaphthenequinone by means of



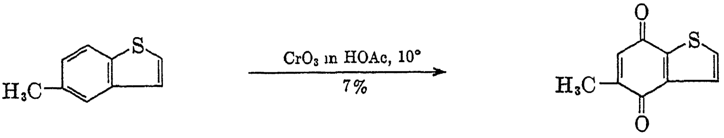
(144)

reaction 144 (184). This compound is alkylated in the 6-position when treated with 4-cyclohexylbutyryl peroxide (642) (eq. 145). This reaction is typical of 1,4-naphthoquinones.

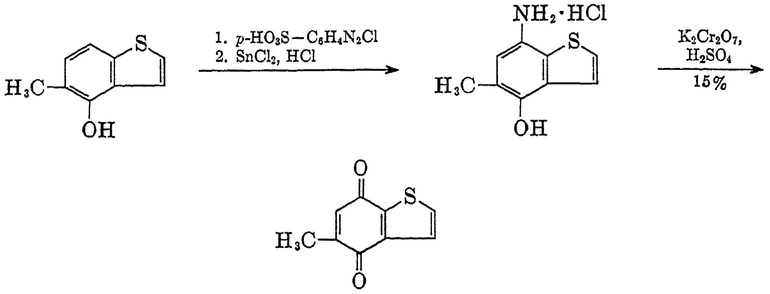


(145)

5-Methyl-4,7-thianaphthenequinone has been prepared in low yield by oxidation of 5-methylthianaphthene with chromic acid anhydride (504) (eq. 146). A somewhat better yield of this compound has been re-



(146)



(147)

ported through a synthesis starting from 5-methyl-4-hydroxythianaphthene (318) (eq. 147).

TABLE II-18. Physical Constants of Benzenoid Thianaphthenequinones and Their Derivatives

Substituents	M.p., °C.	Color	Ref.
	4,5-Thianaphthenequinones		
3-Br	130° (dec.)	Deep violet	222
2-COOH-6,7-di-Cl	227 (dec.)	Dark red	222
2-COOH-6,7-diCl-4,5-dianil	255	Bromine red	222
2-COOH-4,4,6,7-tetra-Cl	213 (dec.)	Yellow	222
2,3,6,7-Tetra-Cl	166	Red	222
2,3,6-Tri-Cl-7-C_6H_5NH	270	Red-brown	222
	6,7-Thianaphthenequinones		
2,5-Di-Cl-3-C_6H_5	186	Red	222
	4,7-Thianaphthenequinones		
None	130–131	Yellow	184
5-CH_3	120–121	Yellow	504,318
6-CH_3	130.5–131.5	Yellow	505
5-OH	204–205	Yellow	184
5-OH-6-CH_3	155–155.5	Yellow	705
3-Br-5-OH-7-anil	213 (dec.)	Deep copper	222
5-CH_3O	205–206	Yellow	184
7(?)-Monosemicarbazone	235 (dec.)	Yellow	184
5-OH-6-$C_6H_{11}CH_2CH_2CH_2$-	104–105	Purple	642

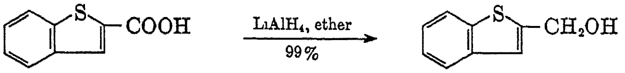
The isomeric 6-methyl-4,7-thianaphthenequinone was obtained in trace yields from 6-methylthianaphthene by oxidation with chromic acid as described in equation 146 (505). The same investigators report that 4,7-thianaphthenequinone cannot be obtained by this method.

The vitamin K activity of 5-methyl-4,7-thianaphthenequinone is only 3% of that of its isolog, 2-methyl-1,4-naphthoquinone (504). Apparently, the vitamin K activity of 6-methyl-4,7-thianaphthenequinone was not measured due to its extremely low yield (505).

5-Hydroxy-6-methyl-4,7-thianaphthenequinone is formed by oxidation of 6-methyl-4-oxo-4,5,6,7-tetrahydrothianaphthene with selenium dioxide in aqueous alcohol solution (705).

VIII. Derivatives Containing Hydroxyl Groups in a Side Chain

Only four investigators have reported compounds of this class. Blicke and Sheets (52) have prepared both the 2- and the 3-thianaphthenylcarbinols. 2-Thianaphthenylcarbinol was prepared by two methods. The best laboratory method appears to be the reduction of 2-thianaphthenecarboxylic acid with lithium aluminum hydride (eq. 148). This compound can also be prepared by reacting thianaphthene with sodium in ether and treating the sodium derivative with monomeric formaldehyde (obtained by heating paraformaldehyde to 180°) (52) (eq. 149).



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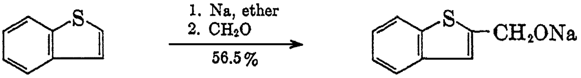
m.p. 99–100°
b.p. 123–125° (1.5 mm.)



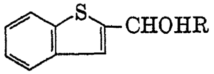
(149)

The benzoate of 2-thianaphthenylcarbinol (b.p. 158–160° (0.02 mm.); m.p. 70–71°) can be obtained by reacting sodium benzoate with 2-chloromethylthianaphthene (90% yield) or by the action of benzoyl chloride on 2-thianaphthenylcarbinol (88% yield) (51a).

3-Thianaphthenylcarbinol is prepared by reduction of the respective 3-thianaphthenecarboxylic acid with lithium aluminum hydride (52). The yield is reported to be 95% of theory. This compound boils at 124–125° at 1.5 mm. and is easily identified as its benzoate; m.p. 92–93°; b.p. 156–158° at 0.02 mm. When treated with dimethylaminoethyl chloride in the presence of caustic, 3-thianaphthenylcarbinol is converted to the corresponding ether (see eq. 70). The simple methyl ether occurs where 3-chloromethylthianaphthene is reacted with sodium methylate (724). It is a liquid, b.p. 118–120° (4 mm.), n_D^{25} 1.6120.

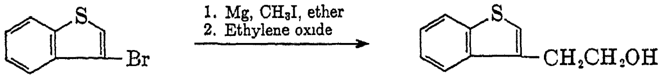
2-Methyl-3-thianaphthenylcarbinol (m.p. 145.8–147.4°) has been obtained by reduction of the corresponding acid with lithium aluminum hydride and by treatment of 2-thianaphthenylmethylmagnesium chloride with monomeric formaldehyde (737). While this Grignard reagent usually rearranges when treated with aldehydes and ketones, benzoyldurene reacts normally and 2-(2-thianaphthenyl)-1-phenyl-1-durenylethanol (m.p. 126.4–127.4°) results. The latter alcohol dehydrates easily at 150° with a trace of iodine catalyst to yield 2-(2-thianaphthenyl)-1-phenyl-1-durenylethylene.

A series of disubstituted carbinols has been synthesized by condensation of 2-thianaphthenyllithium with aldehydes (736). The yields range from 47 to 72% when the aldehydes, RCHO, are employed.



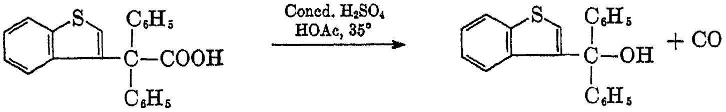
R = CH_3, m.p. 58–58.3°
R = C_6H_5, m.p. 83°
R = p-$CH_3C_6H_4$, m.p. 56.5–57.5°
R = p-ClC_6H_4, m.p. 102–102.5°
R = p-$(CH_3)_2NC_6H_4$, m.p. 137.5–138°

2-(3′-Thianaphthenyl)ethanol is formed by a conventional synthesis from 3-thianaphthenylmagnesium bromide and ethylene oxide (90) (eq. 150). This compound also results in low yield when 3-thianaphthenylacetonitrile is reduced with lithium aluminum hydride; 2-(3′-thianaphthenyl)ethylamine is the principal product (608). The urethan derivative of this alcohol is reported to melt at 105–108°.



(150)

3-Thianaphthenyldiphenylcarbinol results from decarbonylation of 3-thianaphthenyldiphenylacetic acid with sulfuric acid (6) (eq. 151).



(151)

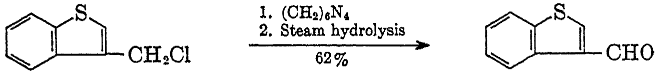
2-Bromo-3-thianaphthenyldiphenylcarbinol, m.p. 166–167°, also has been obtained in this fashion.

IX. Carbonyl Derivatives

A. Thianaphthenecarboxaldehydes

2-Thianaphthenecarboxaldehyde has not been reported. It seems logical to assume that it could be prepared through the condensation of 2-mercaptobenzaldehyde and chloro- or bromoacetaldehyde. This synthesis is conventional for the preparation of 2-keto derivatives of thianaphthene when XCH_2COR is employed. *Note added in proof:* Treatment of 2-thianaphthenyllithium with *N*-methylformanilide is said to give a 62% yield of 2-thianaphthenecarboxaldehyde, m.p. 34–34.5° (777). It can be converted to 2,2′-thianaphthoin, m.p. 154–156°; its thiosemicarbazide melts at 219–220°; its 4′-carboxyanil melts at 300–305°; the 3′-hydroxy-4′ carboxyanil melts at 208.5–209°. Treatment with benzyl cyanide gives 2 (2′-thianaphthenyl)-1-phenyl-1-cyanoethylene, m.p. 127–128°.

3-Thianaphthenecarboxaldehyde can be prepared by the conventional synthesis involving 3-thianaphthenylmagnesium bromide and ethyl orthoformate (329,90). It can also be obtained in good yield from 3-chloromethylthianaphthene and hexamethylenetetramine via the Sommelet reaction (90,533,676) (eq. 152). A somewhat poorer yield is reported by means of the Rosenmund synthesis (176) (eq. 153).



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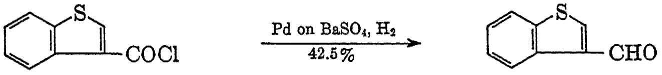
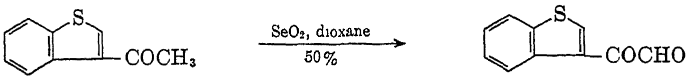


(153)

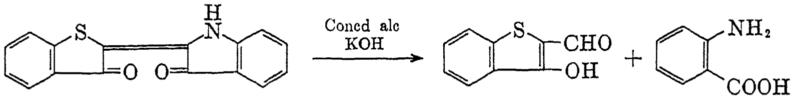
Although direct formylation of thiophene and its derivatives usually leads to high yields of thiophenecarboxaldehydes, King and Nord (621) failed to obtain an aldehyde with thianaphthene. Other investigators (546) employing modifications were able to obtain a 9% yield of a product reported to be 3-thianaphthenecarboxaldehyde when thianaphthene was reacted with *N*-methylformanilide in the presence of phosphorus oxychloride. Although the product melted at 58°, the same melting point as the 3-isomer, the investigators reported that it formed a phenylhydrazone melting at 204–205°. Since other investigators (90) report the melting point of this phenylhydrazone to be 115°, it would appear that this work should be reinvestigated to determine if the direct formylation did not actually yield the 2-isomer rather than the reported 3 isomer.

3-Thianaphtheneglyoxal is formed by oxidation of 3-acetylthianaphthene with selenium dioxide (278) (eq. 154).



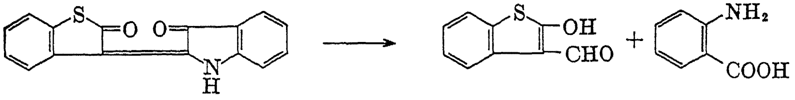
(154)

The only other class of aldo derivatives of thianaphthene known is the hydroxythianaphthenecarboxaldehydes. 3-Hydroxy-2-thianaphthenecarboxaldehyde is obtained from 2-thianaphthene-2′-indoleindigo (204) as



(155)

shown in eq. 155. Similarly, the 2-hydroxy-3-thianaphthenecarboxyaldehyde is prepared from 3-thianaphthene-2′-indoleindigo (200,204) (eq. 156). However, if the isomeric 2-thianaphthene-3′-indoleindigo is employed, the thianaphthene ring ruptured and 2-hydroxy-3-indolecarboxaldehyde is obtained (eq. 157).



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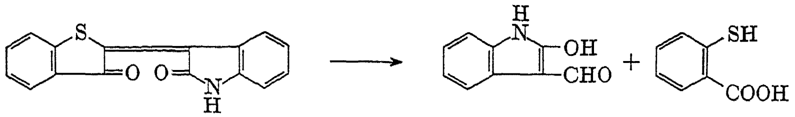
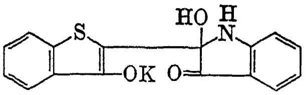


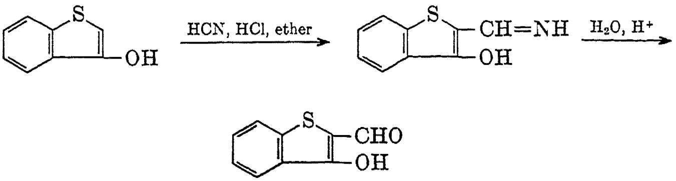
(157)

Although the reasons for this cleavage are not clear, Friedländer (200) indicated that the indole ring rupture took place through an intermediate potassium hydroxide addition complex of the indigo which could be isolated and identified and which was said to have the structure shown in eq. 158 which results from a 1,4-addition of potassium hydroxide.



(158)

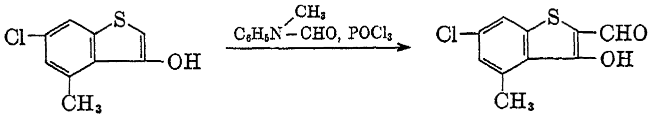
3-Hydroxy-2-thianaphthenecarboxaldehyde can be formed by many of the methods used for the preparation of salicylaldehyde. However, these reactions proceed with 3-hydroxythianaphthene in most cases with considerably greater ease than with phenol. Thus, the Gattermann synthesis used for salicyaldehyde requires anhydrous hydrogen cyanide and hydrogen chloride, with aluminum chloride as a catalyst. Krollpfeiffer *et al.* (334) noted that with 3-hydroxythianaphthene the reaction proceeded to give a good yield of 3-hydroxy-2-thianaphthenecarboxaldehyde without the use of aluminum chloride (eq. 159). These investigators also found



(159)

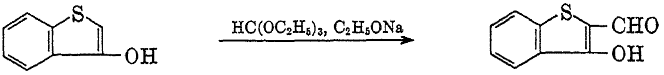
that the 3-methoxythianaphthene was equally active and 3-methoxy-2-thianaphthenecarboxaldehyde could be prepared in the same manner.

Formylation of 6-chloro-4-methyl-3-hydroxythianaphthene with *N*-methylformylanilide is said to take place with considerable ease (P-182) (eq. 160). 6-Ethoxy-3-hydroxy-2-thianaphthenecarboxaldehyde has also been reported to be obtained by this method.



(160)

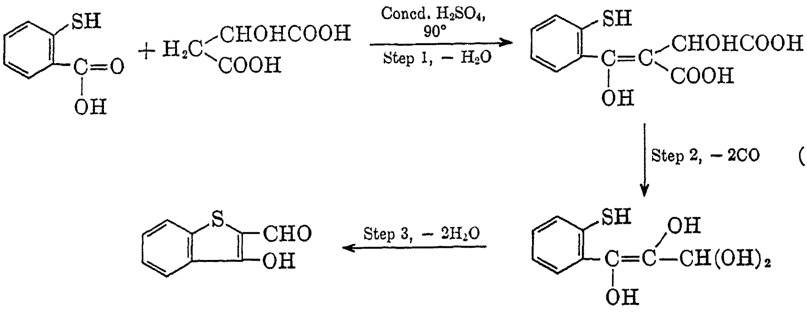
3-Hydroxy-2-thianaphthenecarboxaldehyde can also be obtained from the 3-hydroxy derivatives in a reaction paralleling the Reimer-Teimann reaction (P-138) (eq. 161). The same product is said to be formed from



(161)

carbon tetrachloride instead of ethyl orthoformate (P-138), but the mechanism of such a reaction is not clear. The original of this reference was not consulted, but, presumably, the reaction involves chloroform rather than carbon tetrachloride.

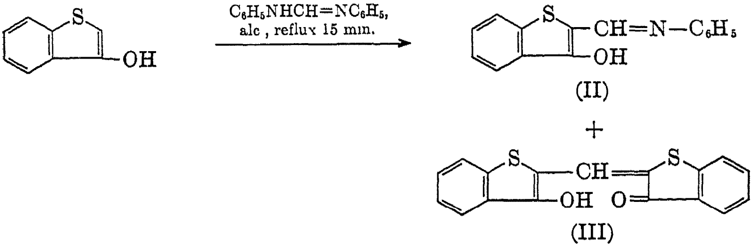
Another method of preparing 3-hydroxy-2-thianaphthenecarboxaldehyde utilizes *o*-mercaptobenzoic acid and malic acid (461). This reaction is rather complex and no attempt will be made to elucidate the mechanism. However, the formation of the final product can be accounted for by reaction sequence 162. Thus, the overall reaction involves the loss of three moles of water and two moles of carbon monoxide. The structure of the resultant product was established by comparison with the product obtained



(162)

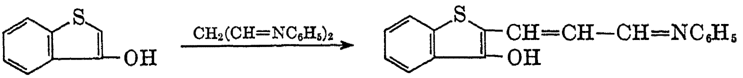
by Friedländer (204) (see eq. 155). Another reaction of this same type requires closure of the thiophene ring by the classical Friedländer method for the preparation of 3-hydroxy-2-thianaphthenecarboxylic acid. In this instance (643), the 2-carboxyphenylthioacetaldehyde is refluxed with acetic anhydride to yield 62% of 3-hydroxy-2-thianaphthenecarboxaldehyde.

3-Hydroxythianaphthene reacts rapidly with diphenylformamidine to yield the anil of 3-hydroxy-2-thianaphthenecarboxaldehyde (497). The reaction is complicated by the interaction of the anil with 3-hydroxythianaphthene to form compound III (eq. 163). Compound II has been formed



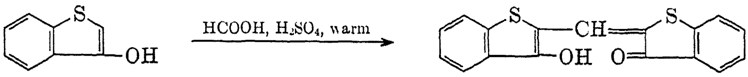
(163)

in another manner by refluxing aniline with 3-hydroxy-2-thianaphtheneglyoxalic acid (216). The method of eq. 163 was extended to the use of the dianil of malonaldehyde and the dianil of glutaconaldehyde (497). In each case, the conjugated olefinic side chain is introduced (eq. 164).



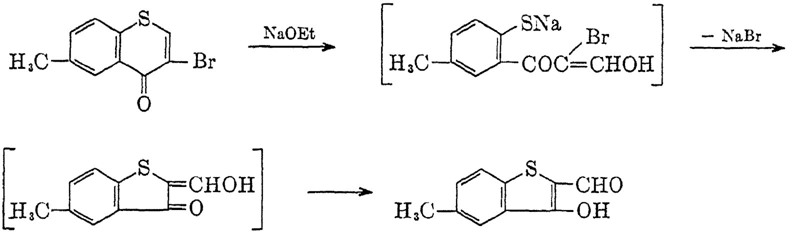
(164)

Still another compound, which involves the formation of 3-hydroxy-2-thianaphthenecarboxaldehyde as an intermediate, is obtained by condensation of 3-hydroxythianaphthene with formic acid (452,643) (eq. 165).



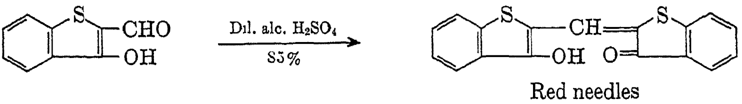
(165)

5-Methyl-3-hydroxy-2-thianaphthenecarboxaldehyde has been synthesized by a rather involved rearrangement of 6-methyl-3-bromobenzothiochromenone in the presence of sodium ethylate (333) (eq. 166).



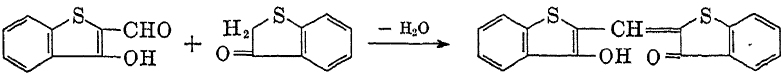
(166)

The hydroxythianaphthenecarboxaldehydes have not been studied to any great extent. However, these compounds appear to undergo typical reactions of both the hydroxyl and the aldehyde groups. The hydroxythianaphthenecarboxaldehydes give characteristic colors with ferric chloride, give a silver mirror test and form the characteristic carbonyl derivatives such as phenylhydrazones (200,204). A rather interesting reaction of 3-hydroxy-2-thianaphthenecarboxaldehyde in alcoholic aqueous sulfuric acid consists of cleavage of one carboxaldehyde group during an internal condensation reaction wherein an indigolone type structure is obtained (204,P-138) (eq. 167).



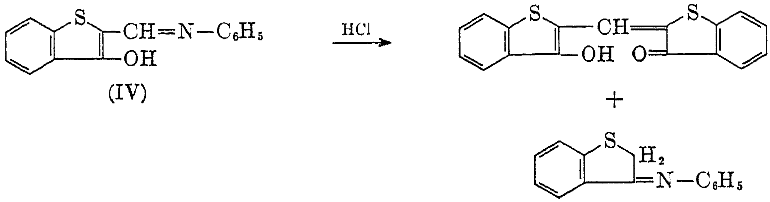
(167)

This same product can be obtained directly by condensation of 3-hydroxy-2-thianaphthenecarboxaldehyde with 3-hydroxythianaphthene in its oxo form (thioindoxyl) (eq. 168). It also is prepared by the action of



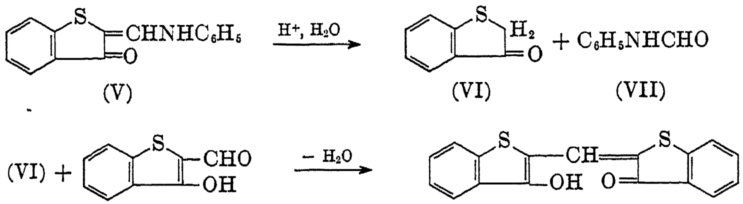
(168)

hydrochloric acid on the anil of 3-hydroxy-2-thianaphthenecarboxaldehyde (216) (eq. 169). Isolation of the anil of the keto form of 3-hydroxythianaphthene indicates that at some point in the reaction the keto form of



(169)

3-hydroxythianaphthene is involved. Conceivably, IV could rearrange to compound V (given below) and hydrolyze to VI (eq. 170). Compound V is known and has been synthesized from VI and VII (315).



(170)

The physical constants of the above-described aldehydes and their derivatives are listed in Table II-19.

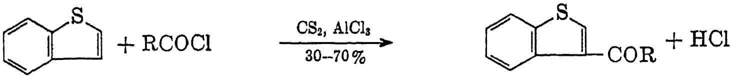
The aldehyde group of this series appears to undergo typical aldehyde reactions with hydroxylamine, semicarbazide, and the hydrazines. 3-Thianaphthenecarboxaldehyde can be nitrated satisfactorily with acetyl nitrate at 0°; the resultant product is the 2-nitro derivative (676). It condenses with benzyl cyanide or arylacetonitriles in the presence of potassium hydroxide to yield β-acrylonitrile derivatives (676). When condensed with benzylmagnesium chloride, 1-phenyl-2-(3′-thianaphthenyl)ethylene results (676). It condenses directly with TNT in benzene and a trace of piperidine to give a quantitative yield of 1-(2′,4′6′-trinitrophenyl)-2-(3′-thianaphthenyl)ethylene.

B. Keto Derivatives of Thianaphthene

Thianaphthene can be acylated in the usual manner with acyl halides employing Friedel-Crafts type catalysts (328,278,80,82,526,99,77). The reaction appears to proceed best in carbon disulfide solvent. The recommended temperature ranges from room temperature to as low as −10° (eq. 171). In the original publication (328) and in reports prior to 1950 (77,80,82,99), no indication of isomer formation was noted. Levine and coworkers (544) have repeated this work on a more precise basis and have found considerable amounts of the 2-isomer. These investigators also

TABLE II-19. Physical Constants of the Thianaphthenecarboxaldehydes and Their Derivatives

Substituents	B.p., °C. (mm.)	M.p., °C.	Deriv.	M.p., °C.	Ref.
3-CHO	149–150 (10)	58			90,329,533,176
	166 (20)				546
	288–289 (741)		Oxime	90	90
			Semicarbazone	235–235.5	90,329,533,176
			Phenylhydrazone	204–205 (115)	546 (329)
			p-Nitrophenylhydrazone	232–233	329
			2,4-Dinitrophenylhydrazone	370	743
2-NO_2-3-CHO	—	124			676
3-COCHO	134–137 (1)		Disemicarbazone	216–218 (dec.)	278
			Di(*p*-nitrophenylhydrazone)	293–295 (dec.)	278
2-CHO-3-OH	—	107	Anil	178–179	497
			Phenylhydrazone	137	204,461,P-138
			Imide	145–150	334
			3-Acetate ester	220	334
2-OH-3-CHO	—	126–127	Aldizine	203	204
				198	643
		130	Anil	179	216
			o-Carboxyanil	249	204
			Semicarbazone	185	643
2-CHO-3-OH-5-CH_3	—	126–127	—	—	333
2-CHO-3-OH-4-CH_3-6-Cl			Aldazine	277–278	P-182
2-CHO-3-OH-6-C_2H_5O			Aldazine	248	P-182
2-CH=CHCHO-3-OH			Anil	217–218 (dec.)	497
2-CH=CH—CH=CH—CHO-3-OH			Anil	201–202 (dec.)	497



(171)

have extended the use of the thiophene acylation catalysts (622) to thianaphthene. Thus they found that thianaphthene can be acylated with acid anhydrides in the presence of iodine, orthophosphoric acid, boron trifluoride complexes, zinc chloride, stannic chloride, and ferric chloride when the catalysts are employed in amounts of the order of 0.01 mole per mole of acid anhydride. When acetic anhydride was employed, both the 2- and 3-acetylthianaphthene were formed. Table II-20 indicates the relative percentages of isomers formed in the acetylation of thianaphthene with these catalysts.

TABLE II-20. Isomer Formation in Acetylation of Thianaphthene

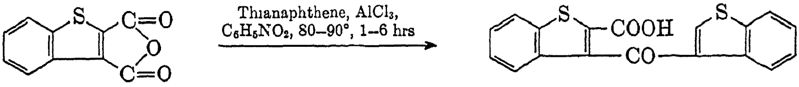
Catalyst[a]	2-Isomer, %	3-Isomer, %	Total yield, %
BF_3 etherate	25	75	67
H_3PO_4	23	77	55
I_2	23	77	63
$ZnCl_2$	29	71	45
$SnCl_4$	33	67	55
$FeCl_3$	28	72	70
$AlCl_3$[b]	12	88	38

[a] Catalyst employed in amounts of the order of 0.01 mole/mole.
[b] Catalyst employed in molecular quantity.

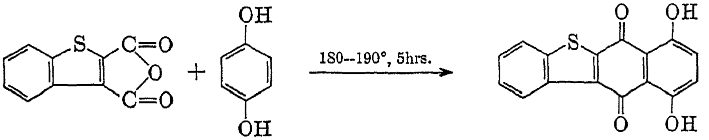
2-Methylthianaphthene yields 3-acyl derivatives when reacted with acyl halides in the presence of stannic chloride catalyst. Boron trifluoride etherate and acetic anhydride gave 3-acetyl-2-methylthianaphthene as well as a product thought to be 2-methyl-1,3-di-(2-thianaphthenyl)propene which resulted from reaction of the 2-methyl groups with acetic anhydride (737). 2-Methyl-3-acyl derivatives also result from the reaction of 2-thianaphthenylmethylmagnesium chloride with acyl chlorides (737). Benzoyldurene did not rearrange and the expected tertiary carbinol, 2-(2-thianaphthenyl)-1-phenyl-1-durenylethanol, was obtained.

Thianaphthene can be acylated with dibasic acid anhydrides such as succinic anhydride (77) and phthalic anhydride (378,P-70,P-419,P-439, P-523). Subsequent ring closure of these materials will be discussed in later chapters under their respective ring systems. The only catalyst effecting the original reaction of the dibasic anhydrides is aluminum chloride; solvents employed were carbon bisulfide and nitrobenzene. A number of catalysts such as sulfuric acid, phosphorus pentoxide, $AlCl_3$-NaCl melts, and stannic chloride are employed in effecting ring closure at the 2-position.

2,3-Thianaphthenedicarboxylic acid anhydride has been employed in a number of acylation reactions with aromatic hydrocarbons (see reference 378 and P-68,P-415,P-416,P-540,P-541), hydroxylated aromatic hydrocarbons 378,P-105,P-421,P-527,P-631), and with thianaphthene (378,P-555). Here again, aluminum chloride was the catalyst. Nitrobenzene, carbon bisulfide, and benzene were used as solvents. The reaction is illustrated in eq. 172 with thianaphthene. The yields from these reactions appear to range from 70 to 90%. When employing the hydroxylated aromatic hydrocarbons, the intermediate ketone is seldom isolated and the end-product is the corresponding condensed system. The best catalyst for this reaction is an aluminum chloride-sodium chloride melt (378,P-527) containing 4 parts of aluminum chloride to 1 part of sodium chloride (eq. 173). 3,3′-Dithianaphthenyl ketone can be isolated as a side product in the formation of 3-thianaphthenecarboxylic acid from 3-thianaphthenylmagnesium bromide and carbon dioxide (329) (eq. 174).



(172)



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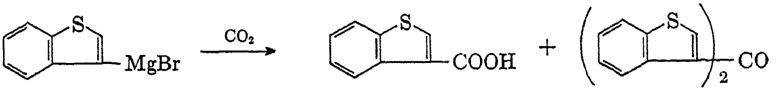
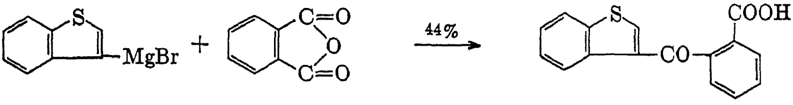


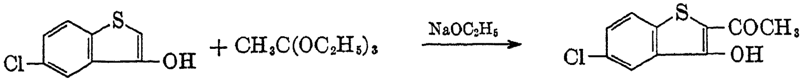
(174)

Komppa (331) added phthalic anhydride to 3-thianaphthenylmagnesium bromide and obtained a 44% yield of 3-(2′-carboxybenzoyl)thianaphthene (eq. 175). The melting point of this product (150.5–151.5°—ref. 331) does not correspond to that report for the product obtained from thianaphthene and phthalic anhydride (175°—ref. 378; 212–214°—ref. P-523). It is possible the compound exists in several isomorphic forms or that the 2-isomer may have been isolated in one of the instances.



(175)

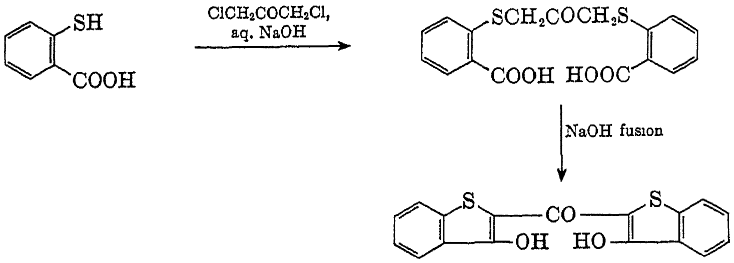
5-Chloro-3-hydroxy-2-acetylthianaphthene results from 5-chloro-3-hydroxythianaphthene and ethyl orthoacetate in a Reimer-Tiemann type reaction (P-138) (eq. 176).



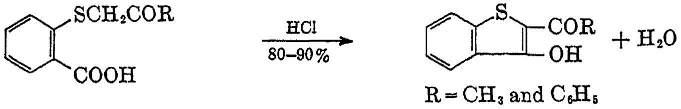
(176)

A somewhat similar synthesis involves the formation of 3-hydroxy-2-thianaphtheneglyoxalic acid from the reaction of 3-hydroxythianaphthene and diethyl oxalate in the presence of sodium ethylate (216).

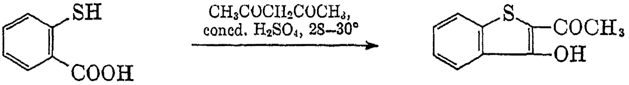
A number of ketone derivatives of thianaphthene have been prepared by a variety of ring-closure methods. The first of these was described by Friedländer (207) (eq. 177). The adaptability of this reaction to simpler ketones has recently been demonstrated by Russian investigators (643), who prepared 2-acetyl- and 2-benzoyl-3-hydroxythianaphthene, effecting the final ring closure with gaseous hydrogen chloride (eq. 178). Another reaction of this type was disclosed by Smiles and McClelland (461) (eq. 179). McClelland and coworkers (191,361,364) studied a somewhat similar reaction of acetic anhydride and chlorobenzisothiazolone in which the 2-acetyl-5-chloro-3-hydroxythianaphthene was obtained along with other 5-chlorothianaphthene derivatives (eq. 180).



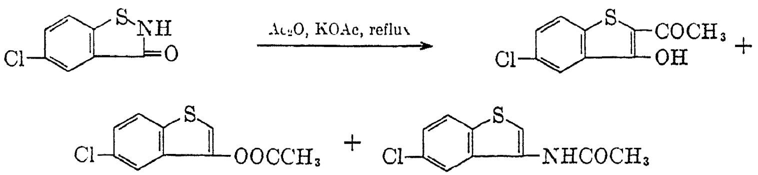
(177)



(178)

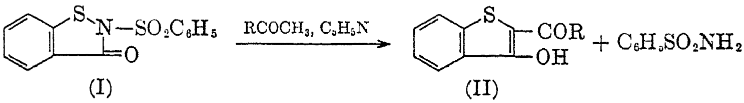


(179)



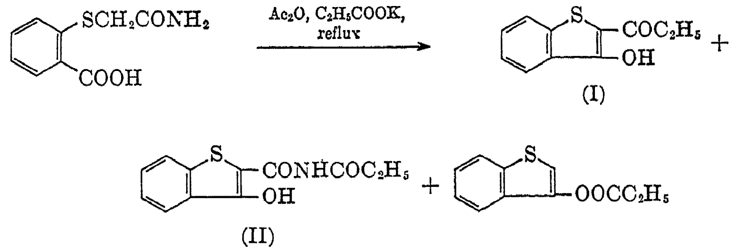
(180)

Barton and McClelland (35) studied the action of compounds containing active methylene groups in this type of reaction and found it to be a general one for the preparation of 2-keto-3-hydroxythianaphthenes (eq. 181). Examples where R = CH_3, C_2H_5, C_3H_7, $COCOOC_2H_5$, and C_6H_5



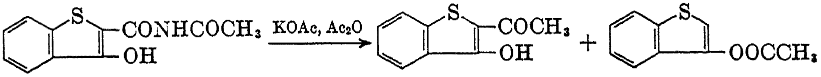
(181)

are listed in the original reference. The physical constants of these compounds are listed in Table II-21. With acetone, however, the yield of 2-acetyl-3-hydroxythianaphthene was very low. The principal product 3,3′-dihydroxy-2,2′-dithianaphthenyl ketone, resulting from the secondary reaction of I and II where R was CH_3 3-Hydroxy-2-propionylthianaphthene is obtained along with two other products as illustrated in eq. 182 (364). The introduction of the —COC_2H_5 group from the potassium



(182)

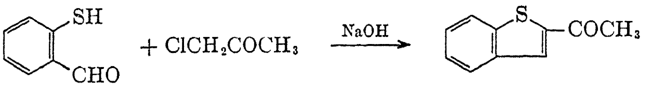
propionate apparently occurs in the same manner as the introduction of —$COCH_3$ group when potassium acetate was reacted with 2-acetylcarbamyl-3-hydroxythianaphthene in boiling acetic anhydride (eq. 183).



(183)

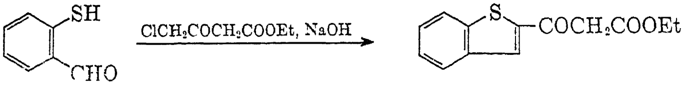
Thus in eq. 182, II apparently was the precursor of I, the latter being formed by the reaction of II and potassium propionate.

The ring closure of *o*-mercaptobenzaldehyde with chloroacetone gives a low yield of 2-acetylthianaphthene (378,749) (eq. 184). Another example



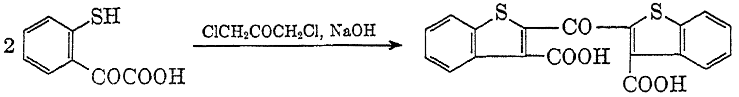
(184)

of this type of ring closure is the condensation of *o*-mercaptobenzaldehyde with ethyl chloroacetate (P-151) (eq. 185). *o*-Mercaptophenylglycolic



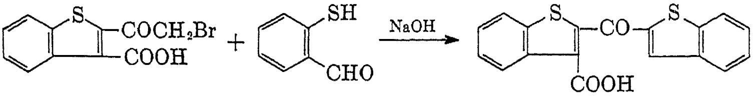
(185)

acid reacts in a similar fashion with *sym*-dichloroacetone to yield 3,3′-dicarboxydi-(2,2′-thianaphthenyl) ketone (P-104,P-555,378) (eq. 186).



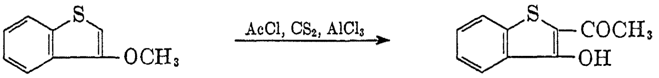
(186)

The monocarboxy derivative of the above ketone is obtained by the condensation of eq. 187 (378).



(187)

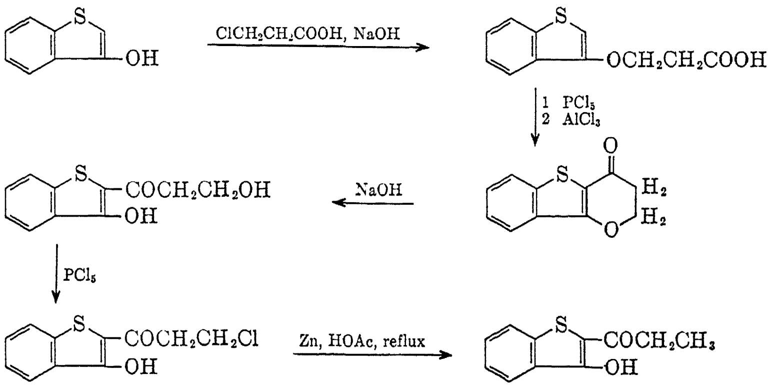
3-Hydroxy-2-acetylthianaphthene can be prepared by direct acylation of 3-methoxythianaphthene (335) (eq. 188). 3-Hydroxy-2-propanoyl-



(188)

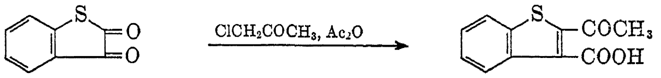
thianaphthene has also been produced by this method. Succinic anhydride with aluminum chloride in tetrachloroethane solvent undergoes a similar reaction with 3-methoxythianaphthene to produce 3(3′-hydroxythianaphthenyl) propionic acid (675).

3-Hydroxy-2-propanoylthianaphthene has been formed by a series of novel reactions (335) (eq. 189). 2,3-Thianaphthenequinones condense with α-halo-ketones in a manner similar to the reaction of the *o*-mercaptophenylglycolic acid. The same end products result (see eq. 186) (378). This

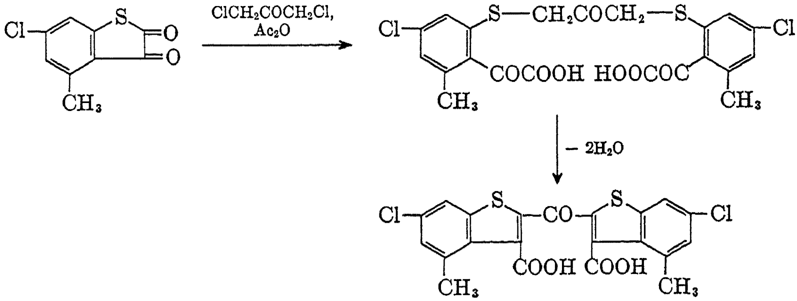


(189)

reaction involves a ring opening and closing similar to that which isatin undergoes in the Pfitzinger reaction. When 2,3-thianaphthenequinone is reacted with chloroacetone, 2-acetyl-3-thianaphthenecarboxylic acid results (378) (eq. 190). Phenacyl bromide employed instead of chloroacetone in the above equation yields 2-benzoyl-3-thianaphthenecarboxylic acid. *sym*-Dichloroacetone reacts with two moles of 6-chloro-4-methyl-2,3-thianaphthenequinone in a similar type reaction to yield the corresponding symmetrical ketone (378,P-104,P-555) (eq. 191). An unsymmetrical 3,3′-dicarboxy-4-methyl-6-chloro-2,2′-di(thianaphthenyl) ketone has been prepared in still another modification of this reaction (378,P-104, P-555) (eq. 192). A series of 2-substituted phenyl derivatives prepared by this reaction is listed in Table II-21. 2-Carboxyphenacyl bromide condenses to yield 2-(2′-carboxybenzoyl)-3-thianaphthenecarboxylic acid



(190)



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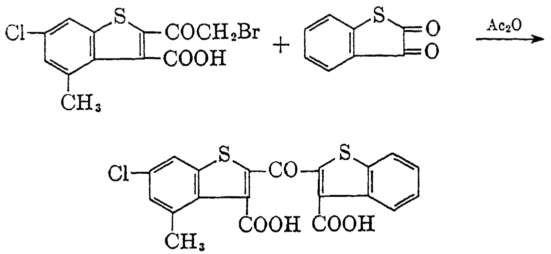
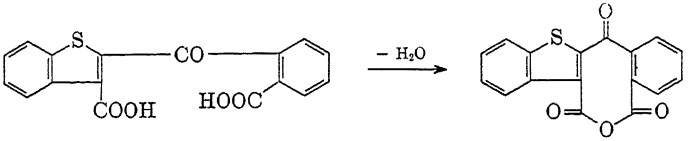


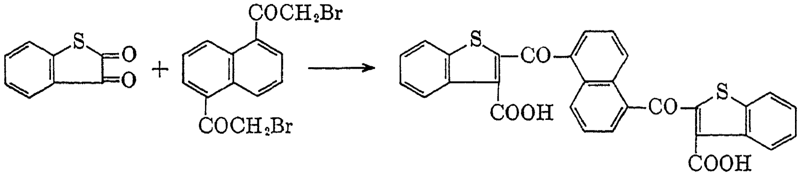
(192)

(378). This compound dehydrates when heated above its melting point to form an 8-membered anhydride ring (eq. 193). 1,5-Di-(ω-bromoacetyl)-



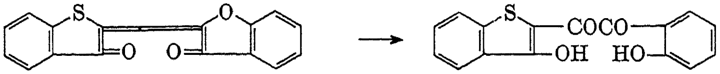
(193)

naphthalene condenses with 2,3-thianaphthenequinone to give 1,5-di(3′-carboxy-2′thianaphthenoyl)naphthalene (378) (eq. 194).



(194)

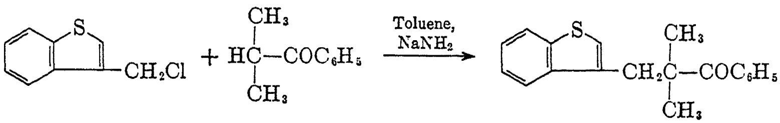
Only one unsymmetrical benzil type compound of the thianaphthene series is reported. 2-Thianaphthene-2′-coumaroneindigo undergoes a ring rupture involving the furanoid ring exclusively when treated with alcoholic sodium hydroxide or with hydrochloric acid in acetic acid (216) (eq. 195).



(195)

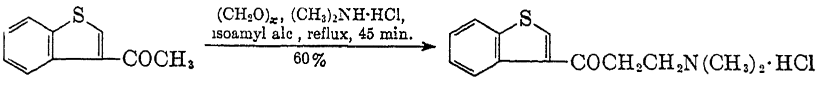
Thianaphthene derivatives with the keto group in the side chain are reported only in one instance (90). The reaction involves the coupling of 3-chloromethylthianaphthene with isobutyrophenone, thus yielding 2,2 - dimethyl - 3 - (3′ - thianaphthenyl)propiophenone (eq. 196). 2,2 -

Dimethyl-4-(3'thianaphthenyl)butyrophenone has been prepared by the same method from 2-(3-thianaphthenyl)ethyl bromide and isobutyrophenone.



(196)

Very few of the reactions of the thianaphthenyl ketones have been studied. Among those investigated is the Mannich reaction of 3-acetylthianaphthene with formaldehyde and dimethylamine hydrochloride (52) (eq. 197). Aromatic aldehydes condense with 2-acetylthianaphthene to give typical benzylidene derivatives (278) (eq. 198). 2-Acetyl-3-hydroxythianaphthene undergoes a similar condensation and a series of dye-like materials related to the indolignones result when salicylaldehyde, *o*-aminobenzaldehyde or *p*-dimethylaminobenzaldehyde is employed (710).



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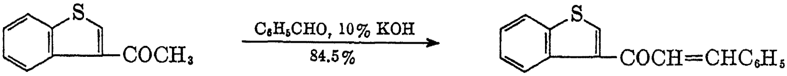
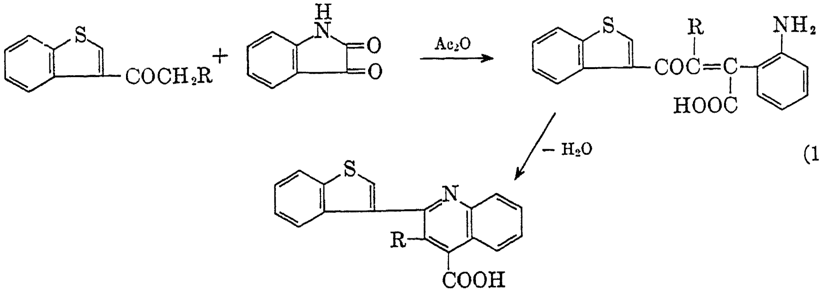


(198)

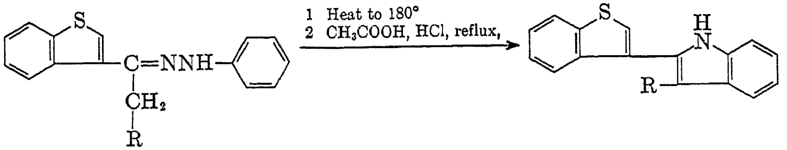
The methyl group of 3-acetylthianaphthene can be oxidized with selenium dioxide to give a 50% yield of 3-thianaphtheneglyoxal (278) (for details see eq. 154). Both 2-acetyl- and 3-acetylthianaphthene condense with ethyl trifluoroacetate in the presence of sodium methylate to give 80–97% yields of the respective 2- and 3-thianaphthenoyltrifluoroacetones (730). Nitration of 3-acyl derivatives with acetyl nitrate is reported to yield 2-nitro derivatives (676). Chlorination in chloroform and carbon tetrachloride solution at room temperature is reported to give a 67% yield of 3-chloroacetylthianaphthene (721).

The Pfitzinger reaction has been studied more thoroughly than any other. The reaction apparently does not proceed as readily as with the corresponding phenyl ketones, but the resultant 3-thianaphthenylcinchoninic acids can be obtained and decarboxylated by standard techniques (76, 77,80,278) (eq. 199). The physical constants of these compounds are listed in Table II-3.



(199)

The Fischer indole synthesis can be carried out with the phenylhydrazones of thianaphthene ketones (86,536). The yields are reported to be quite high (eq. 200). A series of these compounds has been prepared. Their physical constants are listed in Table II-3.



(200)

3-Chloroacetylthianaphthene reacts with sodium sulfide in the usual manner to give bis-(3-thianaphthenacyl) sulfide (55% yield). Oxidation with 30% hydrogen peroxide in acetic acid yields the respective bis-(3-thianaphthenacyl) sulfone (721). 3-Chloroacetylthianaphthene reacts with dithiocarbamate to yield (69%) 4(3-thianaphthenyl)-2-thiazolyl disulfide, m.p. 126–127°. The disulfide is reduced by zinc in acetic acid solution to 4-(3-thianaphthenyl)-2-mercaptothiazole, m.p. 221–223° (721).

The physical properties of the known thianaphthenyl ketones and their derivatives are tabulated in Table II-21.

X. Thianaphthenecarboxylic Acids

A. Monocarboxylic Acids

Both the 2- and 3-thianaphthenecarboxylic acids are prepared easily from thianaphthene. The 2-thianaphthenecarboxylic acids are also readily obtained by ring-closure methods involving *o*-mercaptobenzaldehyde.

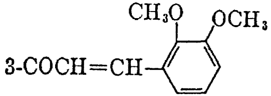
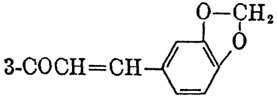
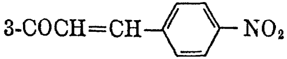
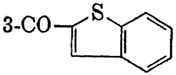
The best synthesis of 2-thianaphthenecarboxylic acid involves direct metalation of thianaphthene with sodium. Subsequent carbonation yields pure 2-thianaphthenecarboxylic acid. No trace of the 3-isomer has been detected. This method was first described by Weissgerber and Kruber

TABLE II-21. Thianaphthene Ketones and Their Derivatives

Substituent	Ref.	B.p., °C. (mm.)	M.p., °C.	Deriv.	M.p., °C.	Ref.
2-$COCH_3$	378,544,749	126–128 (2.5)	87–88	Oxime	187	749
				Semicarbazone	249–250	544
					278	749
				Phenylhydrazone	178	749
2-$COC(CH_3)_3$	749	181 (13)	37	Oxime	199	749
				Semicarbazone	204	749
				Phenylhydrazone	124	749
3-$COCH_3$	328,278,544	135–137 (3)	64–65	Semicarbazone	249–250	544
					244–245	328
		126–128 (2.5)	—	*p*-Nitrophenylhydrazone	223.5–224.5	278
3-$COCH_2Cl$	721	—	139.5–140.5			
3-$COCH_2CH_3$	80,82,99	182–184 (15)	83 (73)	Semicarbazone	202–203	80,82
					204–205	99
3-$COCH_2CH_2CH_3$	80,82	182–185 (10)	95	Semicarbazone	172–173	80,82
3-$CO(CH_2)_3CH_3$	80,82	182–184 (8)	75	Semicarbazone	190–191	80,82
3-$CO(CH_2)_4CH_3$	82	198–205 (10)	96	Semicarbazone	140–141	82
3-$CO(CH_2)_5CH_3$	82	210–215 (10)	94	Semicarbazone	143	82
3-$CO(CH_2)_6CH_3$	82	220–225 (10)	85	Semicarbazone	152	82
3-$CO(CH_2)_7CH_3$	82	227–230 (9)	83–84	Semicarbazone	137	82
3-$CO(CH_2)_8CH_3$	82	240–243 (10)	69–70	Semicarbazone	149	82
3-$CO(CH_2)_9CH_3$	82	245–250 (10)	71–72	Semicarbazone	144	82
3-$CO(CH_2)_{10}CH_3$	82	252–255 (8)	79	Semicarbazone	139	82
3-$CO(CH_2)_{12}CH_3$	82	260–265 (10)	77–78	Semicarbazone	122	82
3-$CO(CH_2)_{14}CH_3$	82	235–250 (0.1)	73	Semicarbazone	109	82
3-$CO(CH_2)_{16}CH_3$	82	250 (0.1)	77	Semicarbazone	104	82
3-COC_6H_5	82	220 (12)	Liquid	Semicarbazone	Does not form	82
3-COC_6H_4-*p*-OCH_3	676	279–285 (13)	112			

Table continued

TABLE II-21 (*continued*)

Substituent	Ref.	B.p., °C. (mm.)	M.p., °C.	Deriv.	M.p., °C.	Ref.
3-COC_6H_4-*p*-OH	676	—	185–187			
3-$COCH_2C_6H_5$	82	—	70	Semicarbazone	200–201	82
2-$COCH_3$-5-C_2H_5	77	185–187 (15)	60–60.5	Semicarbazone	Does not form	77
2-$COCH_3$-3-Cl	748	—	—	2,4-Dinitrophenylhydrazone	238–239	748
2-COC_6H_5-3-CH_3	526	185 (0.09)	58–59			
3-$COCH_2COOC_2H_5$	P-151	—	220–228			
3-$COCH_2CH_2COOH$	77	—	133			
3-$CH_2C(CH_3)_2COC_6H_5$	90	257 (14)				
3-$CH_2CH_2C(CH_3)_2COC_6H_5$	90	265–270 (22)				
3-$COCH{=}CHC_6H_5$	278	—	110–111			
	278	—	119–120			
	278	—	121–122			
	278	—	213.5–214.5			
	329	—	167–167.5			

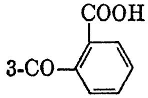
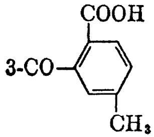
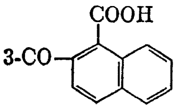
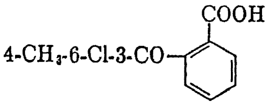
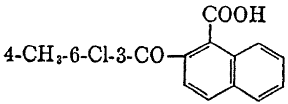
Substituent	Ref.	B.p., °C. (mm.)	M.p., °C.	Deriv.	M p , °C.	Ref
	331,P-70	—	150 5–151 5	Methyl ester	96 5–97.5	331,378
	378	—	175			
	P-523	—	212–214			
	P-68,P-439	—	256–257			
	378	—	180			
	378	—	227–228			
	378	—	244			
2-CH_3-3-$COCH_3$	737	—	69–70			
2-CH_3-3-COC_6H_5	737	—	74.8–76 5			
2-NO_2-3-$COCH_3$	676	—	179			
2-NO_2-3-COC_2H_5	676	—	145			

Table continued

TABLE II-21 (*continued*)

Substituent	Ref.	B.p., °C. (mm.)	M.p., °C.	Deriv.	M p , °C	Ref.
2-NO_2-3-COC_3H_7	676	—	107			
2-$COCH_3$-3-OH	35,361,461, 335,643	—	81	Phenylhydrazone	131	461
				3-CH_3COO	126	643
2-$COCH_3$-3-OH-5-Cl	P-138	—	Not listed			
2-$COCH_2CH_3$-3-OH	35,361,364	183 (15)	73	Semicarbazone	188–189	335
2-$COCH_2CH_2OH$-3-OH	335	—	129–130	Urethan	148–150	335
2-$COCH_2CH_2Cl$-3-OH	335	—	121–122	Phenylhydrazone	167–168	335
				3-Benzoate ester	118–119	335
2-$COCH_2CH_2CH_3$-3-OH	35	—	36			
2-COCOOH-3-OH	35	—	174			
2-$COCH_2CH_2COOH$-3-OH	675	—	190			
2-COC_6H_5-3-OH	35	—	116	3-CH_3COO	105	643
	643	—	118			
2-$COCH_3$-3-COOH	378	—	129–130			
2-$COCH_2Br$-3-COOH	378	—	166–167			
2-$COCH_3$-3-COOH-4-CH_3-6-Cl	378	—	180–181			
2-$COCH_2Br$-3-COOH-4-CH_3-6-Cl	378	—	217–218			
2-COC_6H_5-3-COOH	378	—	240–241			
2-COC_6H_4-*p*-CH_3-3-COOH	378	—	208–209			
2-COC_6H_4-*o*-NO_2-3-COOH	378	—	180–181			
2-COC_6H_4-*m*-NO_2-3-COOH	378	—	204–205			
2-COC_6H_4-*p*-NO_2-3-COOH	378	—	251–252			
2-COC_6H_3-*o*-NH_2-3-COOH	378	—	Not listed	Lactam	312–313	378
2-COC_6H_4-*m*-NH_2-3-COOH	378	—	202–203	*N*-CH_3CO	270–271	378
2-COC_6H_4-*p*-NH_2-3-COOH	378	—	217	*N*-CH_3CO	277	378
2-COC_6H_4-*p*-COOH-3-COOH	378	—	234–235	Anhydride	226–227	378
2-COC_6H_5-3-COOH-6-OC_2H_5	378	—	233–234			
2-COC_6H_5-3-COOH-4-CH_3-6-Cl	378,P-68, P-541	—	256–257 (278)			
2-COC_6H_5-3-COOH-5-Cl-7-CH_3	378	—	252			

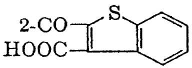
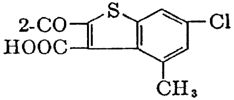
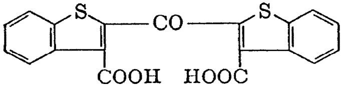
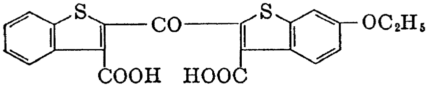
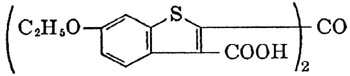
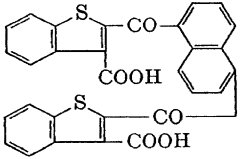
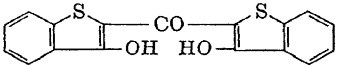
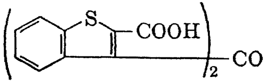
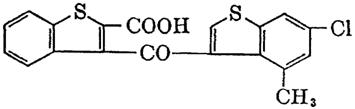
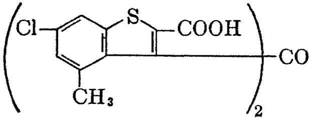
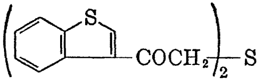
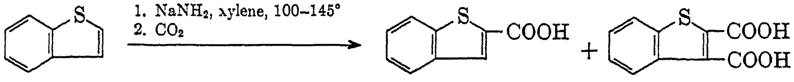
Substituent	Ref.	B.p., °C. (mm.)	M.p., °C.	Deriv.	M p., °C.	Ref.
	378,P-104, P-105, P-555	—	268–269			
	378,P-104, P-555	—	287			
	378	—	228–229	Anhydride Dilactone Phenylhydrazone	265 272–273 180–181	378 378 378
	378	—	247–248	Anhydride	275–278	378
	378	—	164–165			
	378	—	299–300			
	35,207	—	229	Diacetate	182	35,307

Table continued

TABLE II-21 (*continued*)

Substituent	Ref.	B.p., °C. (mm.)	M.p., °C.	Deriv.	M.p., °C.	Ref.
3-COC$_6$H$_5$-2-COOH	378,P-68, P-70, P-415, P-541	—	215–216			
3-COC$_6$H$_4$-*p*-CH$_3$-2-COOH	378	—	199			
3-COC$_6$H$_4$-*p*-Cl-2-COOH	378,P-68	—	198–199			
3-COC$_6$H$_4$-*p*-Br-2-COOH	378	—	220			
3-COC$_6$H$_4$-*p*-OCH$_3$-2-COOH	378	—	195			
	378	—	227–278			
	P-104,P-555	—	272–278			
	P-104	—	Above 340			
2-COOH-2-α-C$_{10}$H$_7$	378	—	Not purified			
2-COOH-3-β-C$_{10}$H$_7$	378	—	Not purified			
	721	—	150–151	Sulfone	236–237	721
2-COCH$_2$COCF$_3$	730	—	96–96.5	Copper salt	319–321 (dec.)	730
				Hydrate	115–116	730
3-COCH$_2$COCF$_3$	730	143–145 (2)	59–60	Copper salt	269–271	730

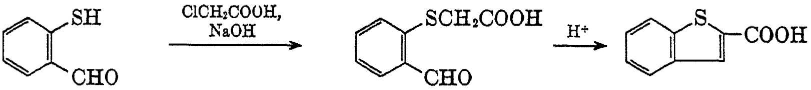
(522,P-387), who reacted thianaphthene with sodamide in liquid ammonia. When the reaction is carried out with a three mole excess of sodamide in xylene, a mixture of 2-thianaphthenecarboxylic acid and 2,3-thianaphthenedicarboxylic acid results (eq. 201). This method has been modified by Schönberg and coworkers (445) and by others (52) to give yields of 50–60% of theory. This modification consists of reacting powdered sodium with thianaphthene in ether solution followed by carbonation. *n*-Butyllithium also reacts to replace the 2-hydrogen. Subsequent carbonation of the 2-thianaphthenyllithium produces a 56% yield of the 2-thianaphthenecarboxylic acid (605). A somewhat lower yield (24%) results when ethylmagnesium bromide is reacted with thianaphthene and the resultant 2-thianaphthenylmagnesium bromide is carbonated (522).



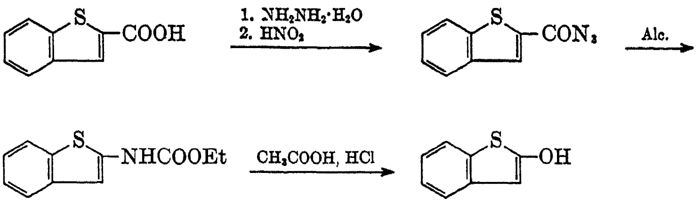
m.p. 236° 30% 8.7% (201)

Farrar and Levine (544) have prepared a sample of this acid from pure 2-acetylthianaphthene via the haloform reaction. Their 2-acid melted somewhat higher (240–241.5°) than previous samples (605) (236–236.5°). The yield from this method is said to be 75% of theory, but this procedure is not to be recommended because of the difficulty in separating the 2- and 3-acetylthianaphthene isomers from the original acetylation reaction.

Friedländer and Lenk (206) formed a compound which also appears to be 2-thianaphthenecarboxylic acid, but the compound melted at 114° (compare to m.p. 236° by Weissgerber and Kruber). This acid was prepared by ring closure of *o*-formylphenylthioglycolic acid and was finally decarboxylated to yield thianaphthene (eq. 202). The structure of Weissgerber and Kruber's acid was established by conversion to 2-hydroxythianaphthene (522) (eq. 203). It is difficult to adjudge these two syn-



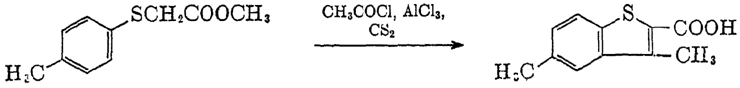
m.p. 114° (202)



(203)

theses, but it would appear that the melting point of the Friedländer and Lenk product indicated impurity. 5-Nitro-2-thianaphthenecarboxylic acid (184,222) has been prepared by the method of Friedländer and Lenk, but the original synthesis does not appear to have been repeated.

A German patent (P-474) describes a method of preparing derivatives of 2-thianaphthenecarboxylic acids substituted in the 3-position by an alkyl or aryl group. The following equation demonstrates the process for the preparation of 3,5-dimethyl-2-thianaphthenecarboxylic acid (eq. 204). Krollpfeiffer and coworkers (574) have demonstrated that this type of synthesis proceeds through an intermediate sulfonium type salt. Thus, the reaction proceeds readily when methyl 2-(*o*-carboxybenzoyl)-4-methylphenyl sulfide is heated in chloroacetic acid, and 3-(*o*-carboxyphenyl)-5-methyl-2-thianaphthenecarboxylic acid results (eq. 205). The original literature should be consulted for more detailed information on this mechanism.



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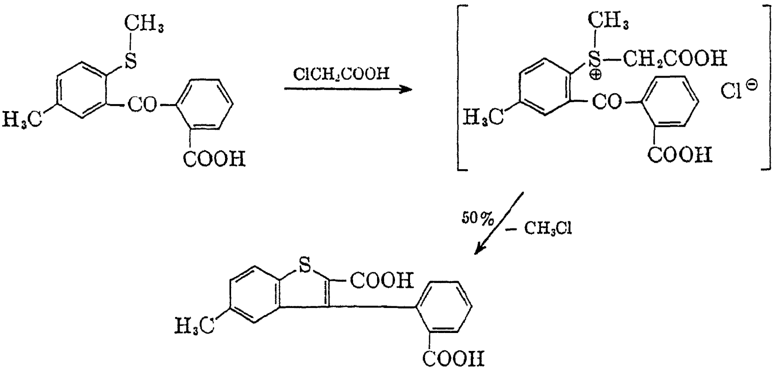
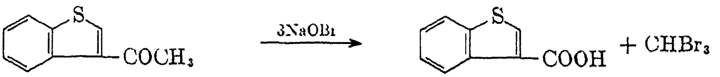


(205)

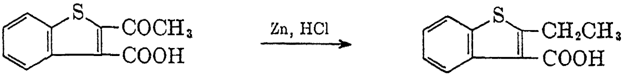
3-Thianaphthenecarboxylic acid has been formed by carbonation of 3-thianaphthenylmagnesium bromide (329,52). This method was also employed to prepare *N*,*N*-diethyl-3-thianaphthenecarboxamide by the coupling action of *N*,*N*-diethylcarbamyl chloride on 3-thianaphthenemagnesium bromide (518). This acid can be obtained from 3-acetylthianaphthene by the haloform reaction (328) (eq. 206). The yield was not



(206)

reported but this reaction normally gives yields of the order of 80% in the naphthalene series. 3-Thianaphthenecarboxylic acid was also prepared by mild oxidation of 3-propanoylthianaphthene with $K_3Fe(CN)_6$ (99).

Only two 2-alkyl-3-thianaphthenecarboxylic acids have been recorded in the literature. 2-Ethyl-3-thianaphthenecarboxylic acid was obtained by reduction of 2-acetyl-3-thianaphthenecarboxylic acid (378) (eq. 207).

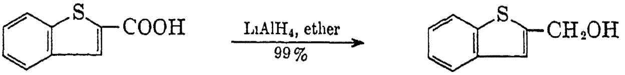


(207)

2-Thianaphthenylmethylmagnesium chloride, when carbonated, yields only a trace of the expected 2-thianaphthenylacetic acid. Instead, the major product is 2-methyl-3-thianaphthenecarboxylic acid (737).

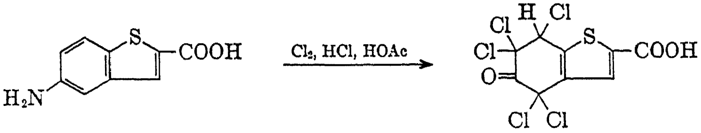
None of the thianaphthenecarboxylic acids with the carboxy group in the benzene portion of the molecule have been reported.

The reactions of the carboxyl group of the thianaphthenecarboxylic acid appear to be those anticipated of an aromatic carboxylic acid and the customary carboxyl derivatives of these acids are tabulated in Table II-22. One very interesting reaction of these acids is the almost quantitative reduction of lithium aluminum hydride to the respective carbinol derivatives (52) (eq. 208). 3-Hydroxymethylthianaphthene was obtained in 96% yield in the same fashion.



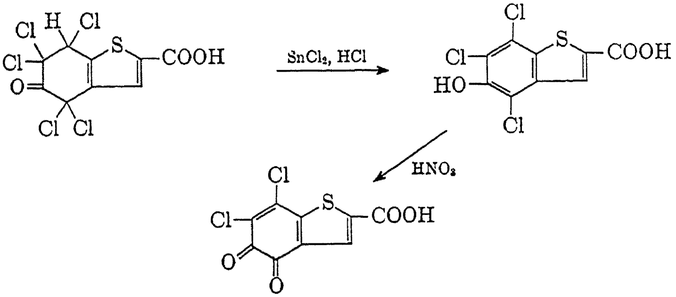
(208)

5-Nitro-2-thianaphthenecarboxylic acid can be reduced conveniently to 5-amino-2-thianaphthenecarboxylic acid in 80% yield (222). This latter compound undergoes an interesting oxidation when chlorinated, and 5 - oxo - 4,4,6,6,7 - pentachloro - 4,5,6,7 - tetrahydro - 2 - thianaphthenecarboxylic acid results (eq. 209). When the above compound is heated



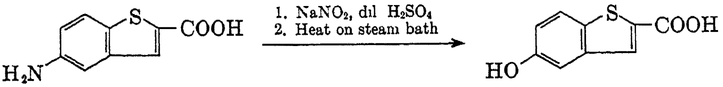
(209)

on a steam bath with dilute acetic acid it loses hydrogen chloride at the 6 and 7 carbons and the chlorines at carbon 4 are hydrolyzed to give 4,5-dioxo - 6,7 - dichloro - 4,5 - dihydro - 2 - thianaphthenecarboxylic acid (222). This same *o*-quinone is obtained by oxidation of 4,6,7-trichloro-5-hydroxy-2-thianaphthenecarboxylic acid which was originally obtained from 5 - oxo - 4,4,6,6,7 - pentachloro - 4,5,6,7 - tetrahydro - 2 - thianaphthenecarboxylic acid (eq. 210). When heated above its melting point,



(210)

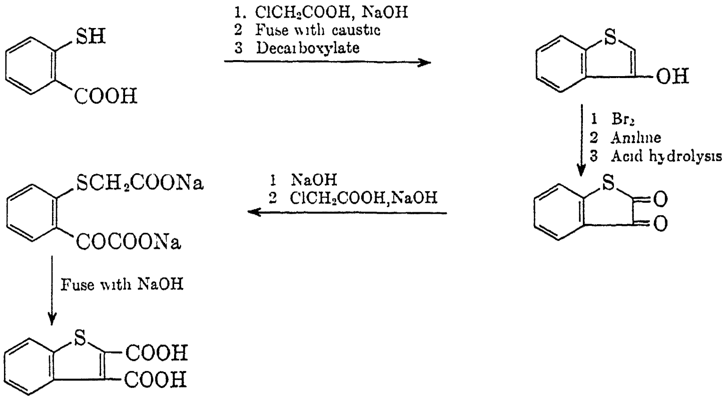
5 - oxo - 4,4,6,6,7 - pentachloro - 4,5,6,7 - tetrahydro - 2 - thianaphthene - carboxylic acid loses one mole of hydrogen chloride at the 6 and 7 carbons to yield 5 - oxo - 4,4,6,7 - tetrachloro - 4,5 - dihydro - 2 - thianaphthene - carboxylic acid (222). 5-Amino-2-thianaphthenecarboxylic acid can be converted to 5-hydroxy-2-thianaphthenecarboxylic acid in low yields (222) (eq. 211).



(211)

B. 2,3-Thianaphthenedicarboxylic Acid and Its Derivatives

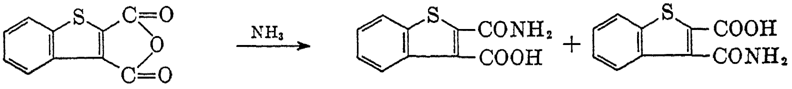
2,3-Thianaphthenedicarboxylic acid is prepared directly from thianaphthene by metalation with sodium followed by carbonation of 2,3-thianaphthenyldisodium with carbon dioxide (522,P-389). The yield is quite low (see eq. 201). The best method involves a multistep reaction starting with *o*-mercaptobenzoic acid (46) (eq. 212). This synthesis appears to have been repeated successfully by Linstead and coworkers (353). Mayer and coworkers (378) prepared 5-chloro-7-methyl-2,3-thianaphthenedicarboxylic acid and 6-ethoxy-2,3-thianaphthenedicarboxylic acid by this method from the respective *o*-mercaptobenzoic acids. Huntress and Olsen (302) were unsuccessful in attempting to prepare 2,3-thianaphthenedicarboxylic acid by the Koelsch-Whitney reaction. Although they were successful in cyclizing diethyl oxalophenoxyacetate to coumarone-2,3-dicarboxylic acid, the analogous diethyl oxalo-(*S*-phenylmercapto)-acetate is so sensitive to this type of cleavage and also loses carbon monoxide so readily that extension of this reaction to the



(212)

preparation of 2,3-thianaphthenedicarboxylic acid was considered to be impractical.

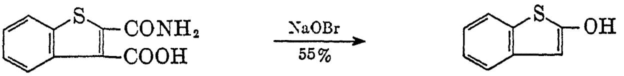
These dicarboxylic acids are very similar to phthalic acid in their ability to lose water and to form anhydrides. Their reactions are essentially the same as those of the phthalic anhydrides. However, they differ in the respect that isomer formation is possible when only one carboxyl group undergoes reaction. For example, it was found that 2,3-thianaphthenedicarboxylic acid anhydride formed two isomeric monoamides when reacted with ammonia (522) (eq. 213). The structures of II and III were proved



(I) (II) (III)

(213)

by a Hoffmann degradation reaction, which resulted in the known 2- and 3-hydroxythianaphthenes (522) (eqs. 214 and 215). The anticipated prod-



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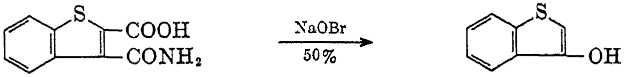
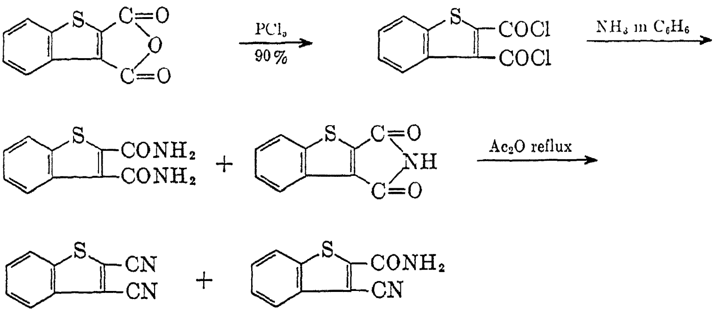


(215)

ucts from the Hoffmann degradation would normally be the respective aminothianaphthenecarboxylic acids, but conditions such as employed in this reaction are somewhat similar to those required for decarboxylation of the 2,3- or 3,2-hydroxythianaphthenecarboxylic acid. It has been demonstrated earlier that the amino group is very readily displaced by a hydroxyl group.

2,3-Thianaphthenedicarboximide is prepared by heating the monocarboxamides (II and III) above 220° (522). A Hoffmann degradation of this compound yields 3-hydroxythianaphthene (eq. 218).

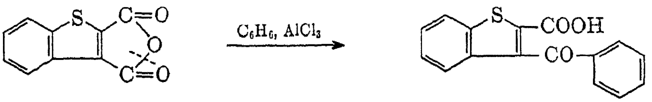
2,3-Thianaphthenedicarboxamide can be obtained as shown in eq. 216 and dehydrated to 2,3-thianaphthenedicarbonitrile (353). The structure of V was not established. Compound IV when heated with aluminum chloride gives a dark-green pigment. Cuprous chloride converts IV to copper tetra-2,3-thianaphthenoporphyrazine, a greenish-blue pigment (for further details see Chapter VIII, section V-b).



(IV) (V)

(216)

Anhydrides of the 2,3-thianaphthenedicarboxylic acids undergo typical reactions of the aromatic dicarboxylic acid anhydrides in the Friedel–Crafts reaction. This reaction and the keto acids derived therefrom are discussed in more detail in section IX.B. The anhydride splits in this case so that the resultant ketone is the 3-isomer (eq. 217). It should be remembered that in the case of the Hoffmann reaction the imide cleaved in the opposite fashion (eq. 218). In this connection it would be an interesting problem to determine how the anhydride ring would cleave in alcoholysis. A determination of the relative reactivity (as well as ionization constants) of the 2- and 3-carboxyl groups is within the realm of possibility and the results should contribute greatly to the fundamental knowledge of the effect



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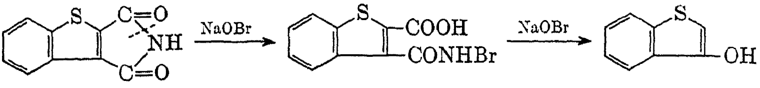
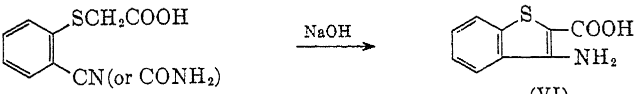


(218)

that such substituents have on the electron distribution within the thiophene ring. For example, it should be possible to react the 2,3-dicarboxylic acid with one mole of silver hydroxide and to prepare the methyl ester by reaction with methyl iodide. A subsequent decarboxylation of the unreacted carboxyl group would lead to the known methyl 2- or 3-thianaphthenecarboxylate.

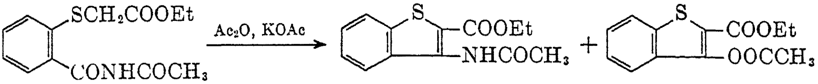
C. 3-Amino-2-thianaphthenecarboxylic Acid

This compound can be prepared by the ring closure of *o*-cyano- (or $CONH_2$)phenylthioglycolic acid by fusion with alkali (197,P-1,P-593, 389,P-272,P-299) (eq. 219). This synthesis has been employed as a route to 3-hydroxythianaphthene in which VI is an intermediate. If, instead of alkali, acid is employed as a condensing agent, or if VI is treated with acid, the resultant product is 3-hydroxy-2-thianaphthenecarboxylic acid. This acid is easily decarboxylated to 3-hydroxythianaphthene. Derivatives of 3-amino-2-thianaphthenecarboxylic acid (VI) result from the ring closure illustrated in eq. 220 (364). Compound VII was successfully saponified to VI.



(VI)

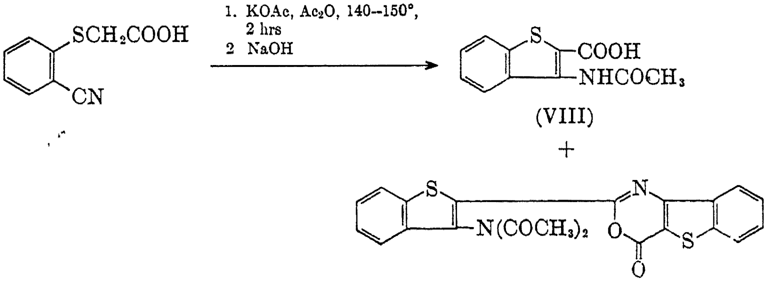
(219)



(VII)

(220)

Another interesting reaction that produces derivatives of VI is a similar type reaction with *o*-cyanophenylthioglycolic acid (363) (eq. 221). If the

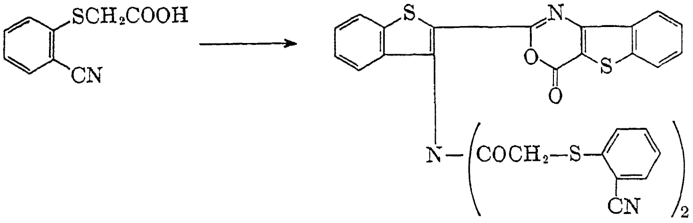


(VIII)

(IX)

(221)

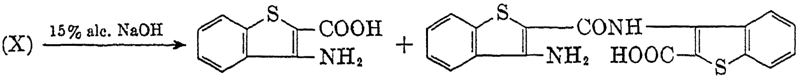
reaction is carried out at 100° for forty minutes, the resultant products are VIII and a derivative of IX (see compound X, eq. 222). Compound X,



(X)

(222)

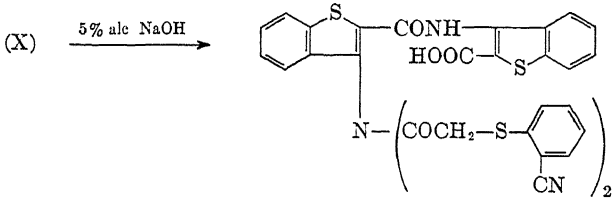
when heated with 15% alcoholic sodium hydroxide, produces VI and an internal amide of VI (eq. 223). However, 5% alcoholic sodium hydroxide



(VI)

(223)

merely cleaves the oxazine ring of X and produces the *N*-monoamide (eq. 224). The action of acetic anhydride on XII causes the formation of the oxazine ring.

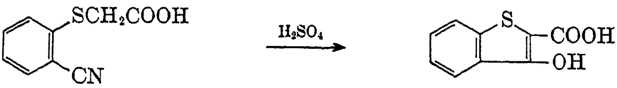


(XII)

(224)

D. 3-Hydroxy-2-thianaphthenecarboxylic Acid

Ring closure of *o*-cyanophenylthioglycolic acid by means of sulfuric acid results in the formation of 3-hydroxy-2-thianaphthenecarboxylic acid (P-593) (eq. 225). This compound also is formed from treatment of

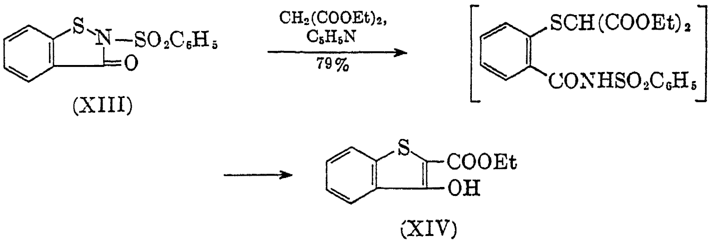


(225)

3-amino-2-thianaphthenecarboxylic acid with dilute mineral acid (P-1) or with sodium hydroxide (P-272). Sulfuric acid (73%) at 170–180° causes ring closure of 3,5-dimethyl-2-carboxyphenylthioglycolic acid and 4,6-dimethyl-3-hydroxy-2-thianaphthenecarboxylic acid results (P-374, P-375).

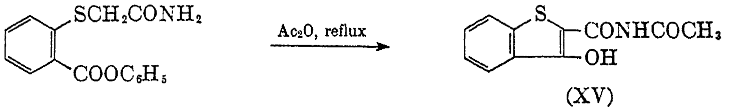
3-Hydroxy-2-thianaphthenecarboxylic acid is also obtained by heating *o*-carboxyphenylthioglycolic acid (197). This material is easily decarboxylated and if the ring closure is carried out in acetic anhydride or sulfuric acid the final product is 3-hydroxythianaphthene (197,P-272).

Another synthesis of this type which probably proceeds through a somewhat similar mechanism is that of Barton and McClelland (35) (eq. 226). XIV also results in 80% yield when XIII is treated with ethyl acetoacetate.

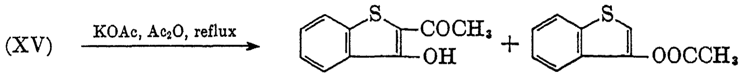


(226)

An amide derivative of 3-hydroxy-2-thianaphthenecarboxylic acid results from the ring closure of *o*-carbophenoxyphenylthioglycolamide by means of acetic anhydride (361) (eq. 227). XV is converted to 2-acetyl-3-hydroxythianaphthene and 3-acetoxythianaphthene by the action of acetic anhydride and potassium acetate (eq. 228).

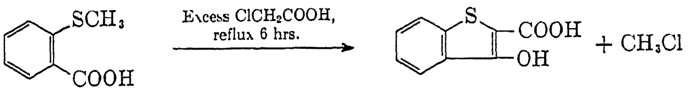


(227)



(228)

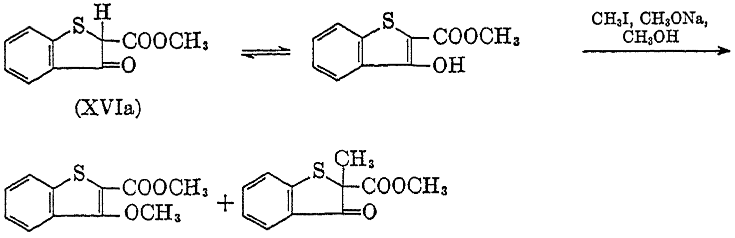
3-Hydroxy-2-thianaphthenecarboxylic acid can be produced in good yields by the versatile synthesis of Krollpfeiffer (573,574) involving ring closure through an intermediate sulfonium salt (eq. 229). Sodium hydrox-



(229)

ide cleaves the acetyl group from XV, yielding 3-hydroxy-2-carbamylthianaphthene.

Auwers studied the tautomerism of methyl 3-hydroxy-2-thianaphthenecarboxylate and found that the keto form was capable of existing, since the compound produced two isomeric products when methylated with methyl iodide (20) (eq. 230). However, when XVIa and XVIb are treated



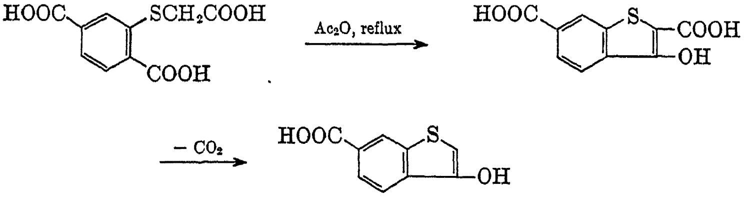
(XVIa)

(230)

(XVIc) (XVId)

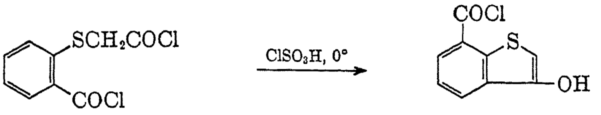
with dimethyl sulfate, only XVIc results. Henecka's (640) study of color reactions of β-diketone systems with ferric chloride indicated by the characteristic blue color that ethyl 3-hydroxy-2-thianaphthenecarboxylate contained a typical —CO$\underset{|}{\text{C}}$HCOOEt structure. Unfortunately, this reaction still cannot give a quantitative estimation of the amount of this form present, but it offers additional proof that both forms may exist in a tautomeric equilibrium.

Acid derivatives of 3-hydroxy-2-thianaphthenecarboxylic acid with the added carboxyl group in the benzene ring are prepared by the standard acetic anhydride ring closure of 2-thioglycoloterephthalic acid (P-441, P-442) (eq. 231). 3-Hydroxy-7-thianaphthenecarbonyl chloride is formed



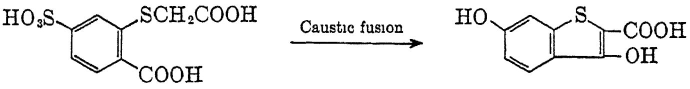
(231)

from *o*-carboxyphenylthioglycolic acid (P-440,P-446,P-119) as shown in eq. 232.



(232)

3-Hydroxy-2-thianaphthenecarboxylic acids with another hydroxyl group in the benzene ring are prepared from the respective sulfonic acid derivatives of *o*-carboxyphenylthioglycolic acids (P-292,P-293,P-294, P-295,P-294a) (eq. 233).

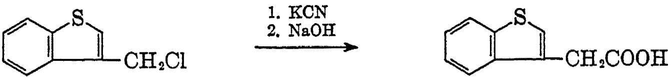


(233)

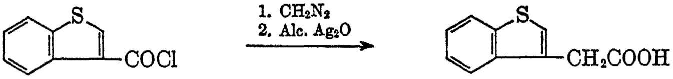
This compound or its 5-isomer (P-294a) can be decarboxylated easily with boiling water to give 3,6- (or 5-) dihydroxythianaphthenes.

E. Thianaphthenecarboxylic Acids with the Carboxyl Group in the Side Chain

3-Thianaphthenylacetic acid can be obtained by conventional syntheses. It is prepared from 3-chloromethylthianaphthene in a two-step reaction involving replacement of the chloride by cyanide and subsequent hydrolysis of the nitrile (27,51a,676) (eq. 234). Blicke and Sheets (52) isolated the 2-isomer in the same fashion from 2-chloromethylthianaphthene in 30% overall yield. 3-Thianaphthenylacetic acid has been made by means of the Arndt-Eistert synthesis from the acid chloride and diazomethane (133,52) (eq. 235). The 2-acetic acid isomer was formed in 74% yield by this method (51a). Prior to the synthesis of 2-thianaphthenylacetic acid (52) by Blicke and Sheets, Crook and Davies (133) had reported the formation of a thianaphthenylacetic acid of unknown constitution from the treatment of ethyl bromoacetate and thianaphthene in the presence of copper powder. Since their compound and that of Blicke and Sheets have the same melting point, it appears that 2-substitution is involved in this reaction. Apparently, this is the only substitution reaction of thianaphthene with the exception

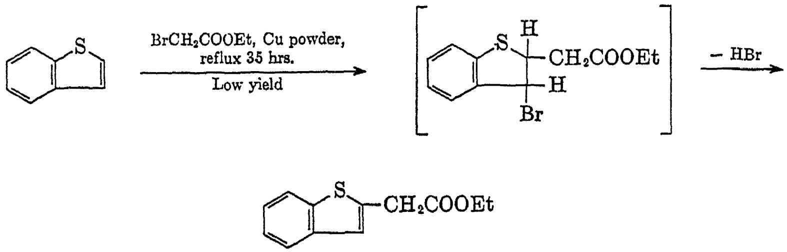


(234)



(235)

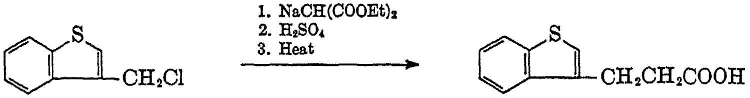
of the metalation, where the entering group attacks the thianaphthene nucleus exclusively at the 2-position. However, it does appear that an addition of the bromoacetic acid to the double bond may have occurred, followed by a dehydrobromination (eq. 236). Further, Crook and Davies (133) reported the formation of a thianaphthenyldiacetic acid (*Authors' note:* probably the 2,3-isomer) by refluxing ethyl bromoacetate with thianaphthene for sixty-four hours with no catalyst.



(236)

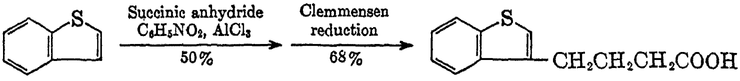
These thianaphthenylacetic acids have considerably less growth-stimulating activity, *i.e.*, as synthetic plant hormones, than α-naphthaleneacetic acid or 3-indoleacetic acid (132,133). The 2,3-thianaphthenyldiacetic acid was reported to have no growth-stimulating activity in the *Avena* test (133).

Diethyl 3-thianaphthenylmethylmalonate has been synthesized by condensation of 3-chloromethylthianaphthene with diethyl sodiomalonate (90). The free acid can be decarboxylated to form 3-(3′-thianaphthenyl)-propionic acid (eq. 237).

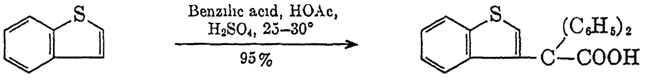


(237)

4-(3′-Thianaphthenyl)butyric acid can be prepared from thianaphthene and succinic anhydride (77) (eq. 238). 3-Thianaphthenyldiphenylacetic acid is reported to form from the condensation of thianaphthene and benzilic acid in the presence of sulfuric acid (6) (eq. 239). Heating of the reaction mixture leads to decarbonylation and 3-thianaphthenyldiphenylcarbinol results. The investigators reported that bromination of XVII yielded a



(238)

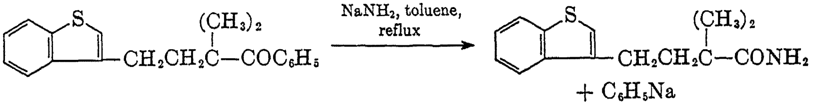


(XVII)

(239)

monobromo derivative, presumably 2-bromo-3-thianaphthenyldiphenylacetic acid. Decarboxylation takes place when the acid (XVII) is heated with potassium hydroxide with the formation of 3-thianaphthenyldiphenylmethane. The preparation of 3-thianaphthenyldi-(*p*-anisyl)acetic acid by the same synthesis (6) has been reported.

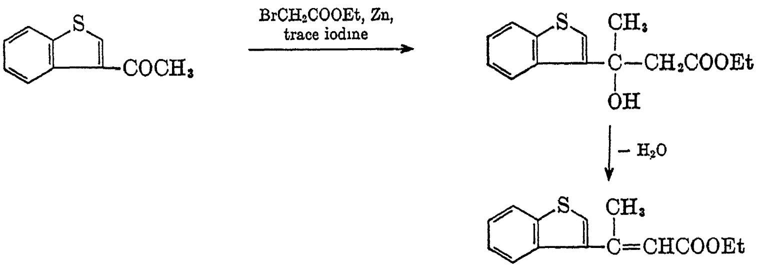
The amides of 2,2-dimethyl-3-(3′-thianaphthenyl)propionic acid and 2,2-dimethyl-4-(3′-thianaphthenyl)butyric acid have been synthesized from their respective benzoyl ketones by cleavage with sodamide (90). Eq. 240 demonstrates the synthesis of 2,2-dimethyl-4-(3′-thianaphthenyl)-butyramide.



(240)

The urine of rabbits fed with thianaphthene contains it only in the form of the thianaphthene-α-glucuronic acid (56). No sulfuric acid esters are produced by rupture of the thiophene ring. The fate of the thianaphthene in the rabbit's body differs from that of benzofuran, which is excreted in forms wherein the furan ring is cleaved.

Miller and Nord (534) have carried out the Reformatsky reaction with 3-acetylthianaphthene. The condensation product, ethyl 3-hydroxy-3-(3′-thianaphthenyl)butyrate dehydrates spontaneously and ethyl 3-(3′-thianaphthenyl)crotonate is the end product of the reaction (eq. 241).



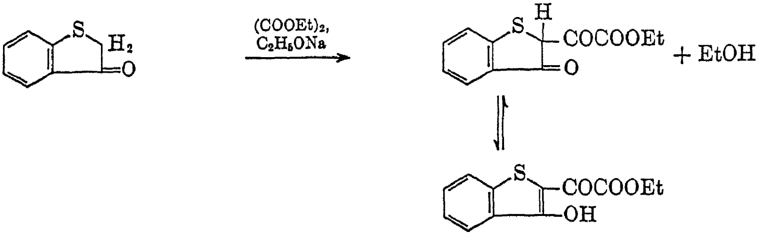
(241)

The end product of the condensation of ethyl 2-bromopropionate and 3-acetylthianaphthene is ethyl 2-methyl-3-(3′-thianaphthenyl)crotonate.

A series of acrylonitrile derivatives of thianaphthene have been prepared (676,743). β-Acrylonitrile derivatives result from condensation of 3-thianaphthenecarboxaldehydes with RCH_2CN, where R is an aryl group. α-Acrylonitriles result when 3-thianaphthenylacetonitrile is condensed with aromatic aldehydes. The physical constants of these materials are appended to Table II-22.

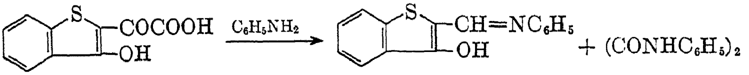
3-Thianaphthenylacetonitrile condenses with *p*-nitrosodimethylaniline through the methylene group in the same fashion as aromatic aldehydes (676). The violet-red crystalline *N*-*p*-dimethylaminophenyl thianaphthenylimidyl cyanide melts at 164°.

Ethyl 3-thianaphthenylglyoxylate is said to form by condensation of thianaphthene with ethyl oxalyl chloride and aluminum chloride (P-705). Ethyl 3-hydroxy-2-thianaphtheneglyoxalate has been synthesized through the condensation of diethyl oxalate with 3-hydroxythianaphthene (216). This reaction appears to be a typical Claissen condensation reaction of the keto form of 3-hydroxythianaphthene although the rearrangement steps are not immediately clear (eq. 242). The free acid when treated with



(242)

aniline undergoes decarboxylation and the products are the anil of 3-hydroxy-2-thianaphthenecarboxaldehyde and oxanilide (eq. 243). The



(243)

anil of the aldehyde results from the usual decarboxylation, but the formation of oxanilide in this reaction is difficult to explain.

3-(3′-Hydroxy-2-thianaphthenoyl)propionic acid has been prepared from 3-methoxythianaphthene by treatment with succinic anhydride and aluminum chloride (675). The simultaneous cleavage of the ether during acylation of the thianaphthene nucleus has been observed previously (335). In the naphthalene series, acylations of methoxy derivatives yields the normal methoxynaphthoylpropionic acids (675).

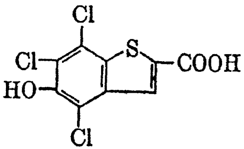
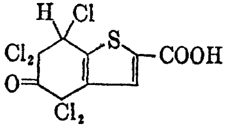
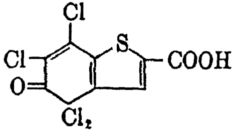
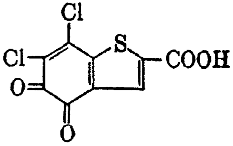
3-Thianaphthenylacetonitrile undergoes a base-catalyzed reaction with diethyl oxalate to yield ethyl cyano-3-thianaphthenylpyruvate (743).

TABLE II-22. Physical Constants of Thianaphthenecarboxylic Acids and Their Derivatives

Compound	M.p., °C.	Deriv.	M.p., °C.	Ref.
2-COOH	240–241.5	—	—	544
	236–236.5	—	—	P-387,52,445, 522,605
	114	—	—	206
		Methyl ester	72–73 B.p. 171 (14 mm.)	522
		Ethyl ester	36–37 B.p. 181–183 (14 mm.)	522
		Acid chloride	88–89 B.p. 173–175 (19 mm.)	522
		Amide	177	522,605
		Hydrazide	184–185	522
		Azide	108	522
		Substituted amides		
		—NHC_6H_5	187 5–188.5	736
		—NH-*o*-$CH_3C_6H_4$	157.5–158	736
		—NH-2-C_5H_4N	132–132.5	736
		—NH-2-C_3H_2NS	194 5–195	736
		—NH-3-pyrimidyl	202–202.5	736
		—NH-3-OH-4-$COOHC_6H_3$	272.5–273	736
		(—NH-*p*-$C_6H_4)_2SO_2$	333 (dec.)	736
3-CH_3-2-COOH	244–244.5			759
5-CH_3-2-COOH	217–218			574
3,5-Di-CH_3-2-COOH	263			P-474
5-CH_3-3-C_2H_5-2-COOH	208–209			574
5-CH_3-3-C_6H_5-2-COOH	260 (dec.)			574
5-CH_3-3-C_6H_4-*o*-COOH-2-COOH	286–287 (dec.)			574
5-NO_2-2-COOH	239–241			184,222
5-NH_2-2-COOH	278 (dec.)	—	—	222
5-OH-2-COOH	264	—	—	222

Table continued

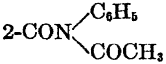
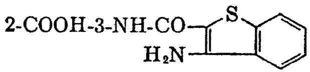
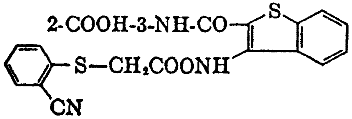
TABLE II-22 (*continued*)

Compound	M.p., °C.	Deriv.	M.p., °C.	Ref.
	290	—	—	222
	172	—	—	222
	213 (dec.)	—	—	222
	227 (dec.)	Dianil	255	222
3-COOH	179–180 174–175 B.p. 305–309°(760)	— —	— —	99,176,328 329,544

Compound	M.p., °C.	Deriv.	M.p., °C.	Ref.
		Methyl ester	B.p. 165–166 (17)	329
			B.p. 285–287 (750)	
		Ethyl ester	B.p. 172–173 (17)	329
			B.p. 304–306 (750)	
		Chloride	50; 53–54	329,133
			B.p. 296–298 (758)	
		Amide	197–198	329
		Azide	176–177	176
		Anilide	172–173	329
		3-(*p*-$CH_3C_6H_4SO_2NHNHCO$—)	201–203	176
		N,*N*-Diethyl amide	B.p. 220 (11)	518
2-CH_3-3-COOH	195.5–196.4	—	—	737
2-C_2H_5-3-COOH	124–125	—	—	378
2,3-Di-COOH	250–251	Dimethyl ester	91	522,378,737
			B.p. 213–215 (18)	
		Anhydride	171	522,353
		Imide	236–237	522
			204–205	353
		2-Carboxamide	221	522
		3-Carboxamide	193	522
		Diamide	240	353
	168–169	—	—	46
	255	—	—	353
		Dinitrile	148	353
		2-Carboxamide-3-nitrile	192–194	353
		Dichloride	70–72	353

Table continued

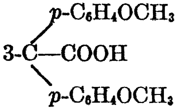
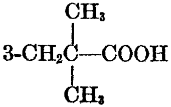
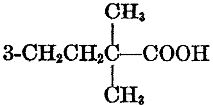
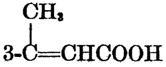
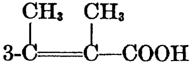
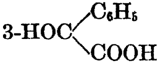
TABLE II-22 (*continued*)

Compound	M.p., °C	Deriv.	M.p., °C.	Ref.
2,3-Di-COOH-5-Cl-7-CH_3	259–260	Anhydride	188–189	378
2,3-Di-COOH-6-C_2H_5O	226	Anhydride	177	378
2-COOH-3-NH_2	140–146 (dec.)	3-CH_3CONH	236	197,363,364, P-272, P-593
		2-$COOC_2H_5$-3-CH_3CONH	—	364
		2-$CONHCOC_2H_5$	188	364
		 $\text{2-CON}\begin{cases}C_6H_5\\COCH_3\end{cases}$	138	364
 2-COOH-3-NH-CO-	246	—	—	363
 2-COOH-3-NH-CO-	260	—	—	363
2-COOH-3-OH	216–217	—	—	574,P-1,P-364, P-593
		N-Methylamide	123	364,34
		N-Ethylamide	133	364
		N-Phenylamide	231	34
		N-Benzylamide	130	364
		Methyl ester	B.p. 148 (20.5)	20
		Ethyl ester	74	35
		2-Ethyl ester-3-acetyl	105	364
		Amide	208	361
		2-Methyl ester-3-methoxy	—	20
		Keto form	74	
		Enol form	68–68.5	

Compound	M.p., °C.	Deriv.	M.p., °C.	Ref.
		2-Methyl ester-3-ethoxy	140	20
		2-$CONHCOCH_3$	204	361
		2-$CONHCOCH_3$-3-$OOCCH_3$	130	361
		3-Methoxy	171–173	20
		3-Ethoxy	158	20
2-COOH-3-OH-4,6-di-CH_3	Not listed	—	—	P-374,P-375
2-COOH-3,5-diOH	Not listed	—	—	P-294a
2-COOH-3,6-diOH	Not listed	—	—	P-293,P-294, P-295
3-OH-6-COOH	250 (subl.)	—	—	P-441,P-442
3-OH-7-COOH	Above 300	—	—	P-440,P-446, P-119
3-OH-4-Cl-6-CH_3-7-COOH	Above 300	—	—	P-446
3-OH-4-C_2H_5O-7-COOH	Not listed	Amide	Not listed	P-446
2-CH_2COOH	141–142	Nitrile	62–64	51a,52,133
			B.p. 129–134 (2)	
		Methyl ester	B.p. 110–114 (0.01)	51a
		Ethyl ester	B.p. 150 (2)	51a
3-CH_2COOH	109	Nitrile	66–67	51a,27,133
			B.p. 138–140 (2)	
		Amide	171–173	51a
2,3-Di-CH_2COOH	108	—	—	133
3-CH_2CH_2COOH	145	Amide	95	90
	B.p. 227 (15)	Nitrile	B.p. 178–180 (22)	90
3-$CH_2CH_2CH_2COOH$	115	Chloride	Oil	77,90
	B.p. 220–222 (3.2)	Amide	130–131	77

Table continued

TABLE II-22 (*continued*)

Compound	M.p., °C.	Deriv.	M.p.· °C.	Ref.
$3\text{-}C(C_6H_5)_2COOH$	244–245 (dec.)	—	—	6
$2\text{-}Br\text{-}3\text{-}C(C_6H_5)_2COOH$	223–224 (dec.)	—	—	6
$3\text{-}CH_2CH(NH_2)COOH$	See Table II-7			
 $3\text{-}C(p\text{-}C_6H_4OCH_3)_2COOH$	245–246 (dec.)	—	—	6
$3\text{-}CH_2CH(COOH)_2$	171 (dec.)	Diethyl ester	B.p. 230 (19) n_D^{20} 1.5424	90
 $3\text{-}CH_2C(CH_3)_2COOH$	—	Amide	103	90
 $3\text{-}CH_2CH_2C(CH_3)_2COOH$	—	Amide	143	90
 $3\text{-}C(CH_3){=}CHCOOH$	149–150	Ethyl ester	B.p. 137–140 (1) n_D^{20} 1 6002	543
 $3\text{-}C(CH_3){=}C(CH_3)COOH$	52–53	—	—	543
$2\text{-}COCOOH\text{-}3\text{-}OH$	—	Ethyl ester	94	216
$2\text{-}COCH_2CH_2COOH\text{-}3\text{-}OH$	190	—	—	675
$3\text{-}CH_2COCOOH$	202	—	—	743
$3\text{-}CH(CN)COCOOH$	—	Ethyl ester	132.5	743
 $3\text{-}HOC(C_6H_5)COOH$	136–137	$HCl\cdot(C_2H_5)_2NCH_2CH_2$ ester	164–165	P-805

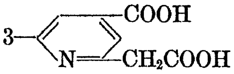
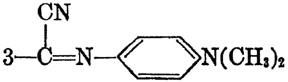
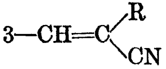
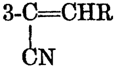
Compound	M.p., °C.	Deriv.	M.p., °C.	Ref.
	Above 320	—	—	77
	155 (164)	—	—	743 (741)
	—	—	—	676
R = C_6H_5	132			
R = p-$CH_3C_6H_4$	139			
R = p-$C_2H_5C_6H_4$	115			
R = p-ClC_6H_4	180			
R = p-BrC_6H_4	178			
R = p-$CH_3OC_6H_4$	118	—	—	676
	119.5	—	—	743
R = p-HOC_6H_4	202			
R = p-$NO_2C_6H_4$	209			
R = α-$C_{10}H_7$	144			
R = β-$C_{10}H_7$	179			
R = 2-CH_3O-1-$C_{10}H_6$	147			
R = 2-C_4H_3S	105	—	—	676,743
R = 3-Thianaphthenyl	203			
R = 5-Indanyl	145	—	—	743
 $3\text{-}\underset{\displaystyle CN}{\underset{\vert}{C}}{=}CHR$	—	—	—	676
R = C_6H_5	114 (110)	—	—	(743)

Table continued

TABLE II-22 (*continued*)

Compound	M.p., °C.	Deriv.	M.p., °C.	Ref.
R = p-ClC_6H_4	146			
R = p-FC_6H_4	154			
R = m-$NO_2C_6H_4$	150			
R = o-$CH_3OC_6H_4$	125 (121.5)	—	—	(743)
R = p-$CH_3OC_6H_4$	97 (91)	—	—	(743)
R = p-HOC_6H_4	184			
R = 3,4-DiCl-C_6H_3	153			
R = 2,4-DiCl-C_6H_3	142			
R = 3,5-DiCl-C_6H_3	143			
R = 3,4-$(HO)_2C_6H_3$	155			
R = 5-Cl-2-$CH_3OC_6H_3$	146			
R = 5-Br-2-$CH_3OC_6H_3$	164			
R = α-$C_{10}H_7$	138 (140)	—	—	(743)
R = 2-CH_3O-1-$C_{10}H_6$	151			
R = β-$C_{10}H_7$	148			
R = 3-Acenaphthenyl	176			
R = 9-Anthryl	220			
R = 3-Pyrenyl	231			
R = 2-Furyl	94 (91)	—	—	(743)
R = 2-Thienyl (C_4H_3S)	124 (120)	—	—	(743)
R = 5-CH_3-2-C_4H_2S	134			
R = 2,5-$(CH_3)_2$-3-C_4HS	123			
R = 5-Cl-2-C_4H_2S	185			
R = 5-Br-2-C_4H_2S	183			
R = 3,4-Dioxymethylenephenyl	112 (109)	—	—	(743)
R = $C_6H_5CH{=}CH$	135.5	—	—	743
R = 3-Thianaphthenyl	191	—	—	743

Acid hydrolysis causes the resultant dibasic acid to decarboxylate yielding 3-thianaphthenylpyruvic acid.

3-Thianaphthenylmagnesium bromide reacts with mandelic acid to yield phenyl-3-thianaphthenylglycolic acid (P-685). The same compound results when phenylmagnesium bromide is condensed with 3-thianaphthenylglyoxalic acid (P-685).

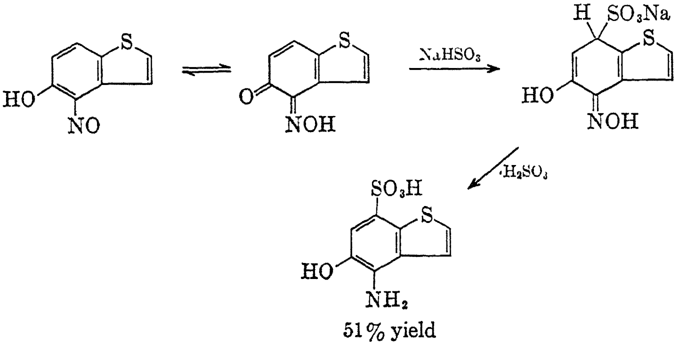
XI. Thianaphthenesulfonic Acids and Thianaphthene Sulfides

An extremely limited amount of work has been reported on this class of thianaphthene compounds. Here, certainly, is a promising field for future research. No thianaphthenethiols have been reported. Two sulfides have been synthesized but no disulfides, sulfoxides, or sulfones are reported. The sulfonation of thianaphthene has been investigated only in a perfunctory manner and the actual position of the entering sulfonyl group has not been determined. The assumption is made that sulfonation occurs predominately at the 3-position which is similar to other electrophilic substitutions.

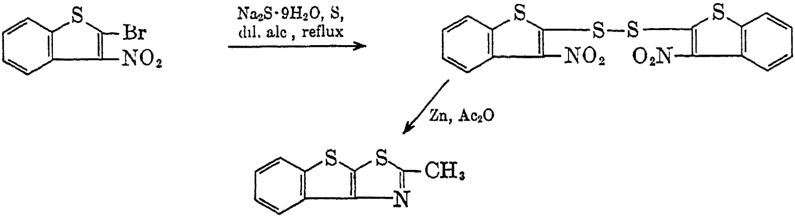
Weissgerber and Kruber (522) in 1920 described the separation of thianaphthene from coal tar naphthalene by sulfonation. The reaction was not totally selective and it was quite difficult to prepare pure thianaphthene in this manner. Later, Weissgerber (P-390) described a process for the production of 3-thianaphthenesulfonic acid by sulfonating in acetic anhydride solution. The sulfonic acid was a partially crystalline, syrupy liquid which decomposed on heating with dilute sulfuric acid at 140° to thianaphthene and sulfuric acid. Komppa (328) was able to sulfonate thianaphthene with 75% sulfuric acid at low temperatures to yield a monothianaphthenesulfonic acid which was isolated as the crystalline sodium salt. In addition, he reported that a small amount of disulfonic acid, isolated as the disodium salt, was formed in the reaction. This latter compound could also be prepared in higher yields by a subsequent sulfonation of the monosulfonic acid.

Only one sulfonic acid derivative with the acid group in the benzene ring has been reported. It has been prepared by a 1,4-addition of sodium bisulfite to the quinone form of 5-hydroxy-4-nitrosothianaphthene (184) (eq. 244).

Middleton and Dawson (P-598) reported that the isomeric bromonitrothianaphthenes reacted easily with dilute alcoholic solutions of sodium disulfide to produce the isomeric dithiobisnitrothianaphthenes. For example, 2-bromo-3-nitrothianaphthene yields 2,2′-dithiobis-(3-nitrothianaphthene). This compound when reduced with zinc and acetic anhydride yields 2-methylthianaphtheno[2,3-*d*]thiazole (eq. 245). This thiazole derivative and its β-isomer are discussed in greater detail in Chapter VIII.



(244)

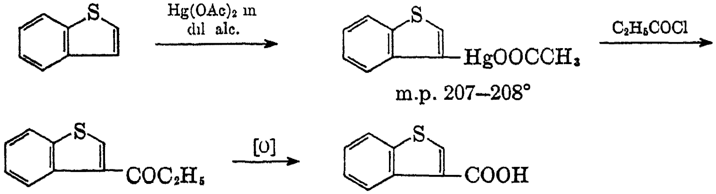


(245)

XII. Mercury Derivatives

Bezdrik, Friedländer, and Königer (46) discovered that thianaphthene reacted with mercuric acetate in acetic acid or alcohol to give one or more mercuriacetates. Weissgerber and Kruber (522) separated thianaphthene from naphthalene by means of the selective reaction of thianaphthene with mercuric acetate in methyl alcohol solution. This same method was used to determine the presence of thianaphthene in Kimmeridge shale oil (98).

Challenger and Miller (99) have undertaken the only systematic study of the mercuration of thianaphthene. These investigators found that a monomercuriacetate of thianaphthene was formed by the reaction of mercuric acetate in very dilute alcohol solution. The position of substitution of the mercuriacetate group was established by reacting this derivative with propionyl chloride and oxidizing the resultant ketone to 3-thianaphthenecarboxylic acid (eq. 246). When the mercuration is carried out

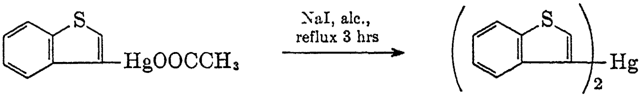


(246)

in aqueous methanol and acetic acid, a mixture of 3-thianaphthenemercuriacetate and a dimercuriacetate is formed. Presumably, this is the 2,3-thianaphthenedimercuriacetate isomer.

Challenger and Miller (99) were not successful in preparing a monomercurichloride derivative. Instead, only the dimercurichloride derivative, m.p. 274–281°, could be isolated. Apparently this is the 2,3-thianaphthenedimercurichloride isomer.

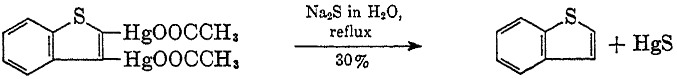
Di-(3-thianaphthenyl)mercury, m.p. 322°, is prepared by reacting 3-thianaphthenylmercuriacetate with sodium iodide (eq. 247). This



(247)

mercury derivative was also obtained when attempts to convert the mercuriacetate to the corresponding chloride was carried out with calcium chloride.

The monomercuriacetate derivative can be split with acid and thianaphthene can be recovered in good yields (522). The dimercuriacetate is split with an excess of sodium sulfide in water and thianaphthene is regenerated (90) (eq. 248). Another compound, m.p. 292–293°, which



(248)

may have been an impure sample of di-(3-thianaphthenyl)mercury (*Authors' Note:* may also be the 2-isomer), has been obtained in this reaction.

Additional mercury derivatives of halothianaphthenes and halothianaphthene 1-dioxides have been prepared by Lampert (748). Physical constants of these compounds are listed in tables of those sections.

XIII. Thianaphthene 1-Oxides (Sulfoxides)

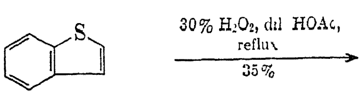
Thianaphthene 1-oxide is unknown. Normal oxidation of thianaphthene with hydrogen peroxide in acetic acid solution yields the sulfone. When thianaphthene is treated with chlorine in carbon tetrachloride and water at 0°, 2,3-dichloro-2,3-dihydrothianaphthene 1-oxide results (m.p. 158–159°) (748). Controlled oxidation of 2,3-dibromothianaphthene with hydrogen peroxide in acetic acid yields the corresponding 1-oxide (m.p. 156.5–157.5°) (748). 2-Bromo-3-chlorothianaphthene 1-oxide (m.p. 141–143°) results from like treatment of 2-bromo-3-chlorothianaphthene.

2,3-Dibromothianaphthene 1-oxide reacts with amines to yield 3-amino derivatives (748). The 3-morpholino- (m p. 161° (dec.) and 3-piperidino- (m.p. 147–148° (dec.)) derivatives have been prepared.

XIV. Thianaphthene 1-Dioxides (Sulfones)

A. Preparation

Thianaphthene 1-dioxide was first prepared by Lanfry (342), who treated thianaphthene with hydrogen peroxide in acetic acid solution (eq. 249). The same method has been employed by other investigators to

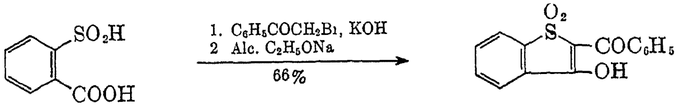


(249)

prepare this compound (61,62,100) and its 3-bromo- (59), 5-nitro- (60), 5-methyl- (504), 3-hydroxy- (343,359,14), 3-hydroxy-2-methyl- (359), 5-chloro-3-acetoxy- (190), 2-methyl-3-propionoxy- (359), and 3-carboxy- (133) derivatives. The yields are of the order of 85% rather than the 35% reported by Lanfry.

Lanfry (343) and later Posner and Wallis (410) studied the action of oxidizing agents on the colors of thioindigo. Lanfry obtained a thioindigo of carmine red color by oxidation of 3-hydroxythianaphthene with hydrogen peroxide. Subsequent treatment with additional hydrogen peroxide cleaved the indigo structure to yield 3-hydroxythianaphthene-1-dioxide. Posner and Wallis (410) found that thioindigo with oxidizing agents yielded two compounds, $C_{16}H_8O_3S_2$ and $C_{16}H_8O_4S_2$, which they described as a monosulfoxide and a monosulfone, respectively.

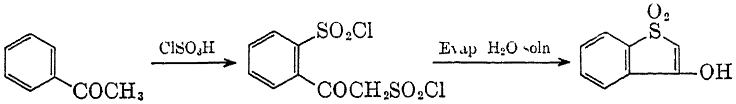
Several sulfones have been prepared by ring-closure methods applicable to the preparation of the hydroxythianaphthenes. For example, *o*-carboxyphenylsulfinic acid can be reacted with phenacyl bromide and subsequently ring closed to produced 2-benzoyl-3-hydroxy thianaphthene 1-dioxide (114) (eq. 250). A similar synthesis was carried out with *p*-



(250)

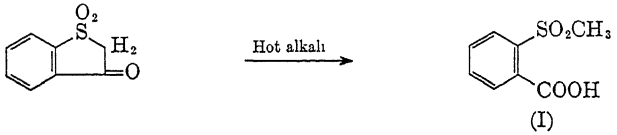
nitrobenzyl bromide and *o*-carboxyphenylsulfinic acid to prepare 2-(*p*-nitrophenyl)-3-hydroxythianaphthene 1-dioxide (415). Arndt and coworkers (14) prepared 2-carbethoxy-3-hydroxythianaphthene 1-dioxide by a conventional ring closure of the sulfone of *o*-carboxyphenylthioglycolic acid.

Weston and Suter (527) prepared 3-hydroxythianaphthene 1-dioxide from acetophenone as in eq. 251. These investigators (527), as well as



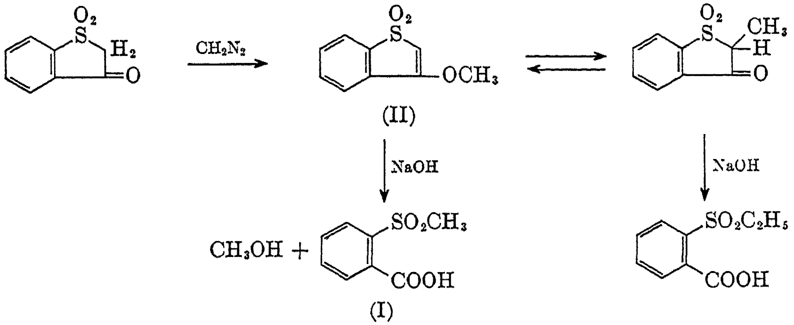
(251)

others (14), considered the possibility that 3-hydroxythianaphthene 1-dioxide and its derivatives existed predominantly in the keto form, since hot caustic solutions cleaved the molecule into *o*-carboxyphenyl methyl sulfone (eq. 252). It was even considered that 2-carbethoxy-3-hydroxy-



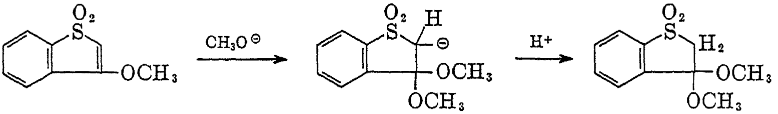
(252)

thianaphthene 1-dioxide which could easily be decarboxylated in hot sulfuric acid to give the 3-hydroxy derivative, existed in the keto form to a major extent, since hot alkali cleavage yielded both *o*-carboxyphenyl methyl sulfone and the sulfone of *o*-carboxyphenylthioglycolic acid. Still other evidence, not particularly supporting either the keto or the enol form, was presented by Arndt and Martius (16). They formed the 3-methoxy derivative by treatment with diazomethane, but found that it, too, cleaved with caustic to give *o*-carboxyphenyl methyl sulfone (I). However, the compound was observed to react with sodium in methanol to give a compound described as a dimethyl acetal of the parent compound. Both the monomethyl and the dimethyl derivatives were converted to the parent compound by means of concentrated hydrochloric acid. It should be pointed out that if the methyl group of the methoxy derivative (II) had migrated to the 2-position prior to ring cleavage the product should have been *o*-carboxyphenyl ethyl sulfone (eq. 253). Actually, only I was



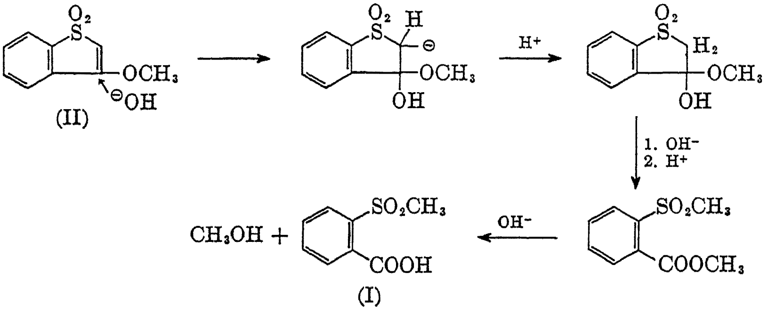
(253)

obtained. Therefore, it seems probable that if a dimethyl acetal derivative of the parent compound formed, it occurred by addition of methyl alcohol across the double bond (eq. 254). Treatment of either the ether or the acetal should regenerate the parent sulfone.



(254)

The mechanism for the cleavage is believed to be quite similar to acetal formation, involving an initial attack by a hydroxyl ion rather than a methoxyl ion, and is simply a reversal of the ring-closure reaction (*i.e.*, addition of water to cleave the double bond at carbon 2 and 3 where water was originally removed to effect closure) (eq. 255).



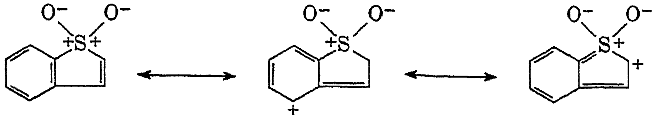
(255)

3-Hydroxythianaphthene 1-dioxide reacts with phenylhydrazone in the same manner as 3-hydroxythianaphthene to form a phenylhydrazone. This phenylhydrazone differs from the phenylhydrazone of 3-hydroxythianaphthene in that the expected Fischer indole ring closure does not take place (360). This ring closure is reported in detail in Chapter VIII.

Feist (181) sulfonated ethyl benzoylacetate with fuming sulfuric acid and obtained a minor amount of 3-hydroxythianaphthene 1-dioxide and a compound shown by later investigators (14) to be 2-carbethoxy-3-hydroxythianaphthene 1-dioxide. The acid chloride of this latter compound, when treated with aqueous ammonia, yielded a compound thought by the investigators to be 3-amino-2-carbamylthianaphthene 1-dioxide (m.p. 315°) along with another product of doubtful structure which might possibly have been 3-amino-2-carbethoxythianaphthene 1-dioxide (m.p. 233–234°).

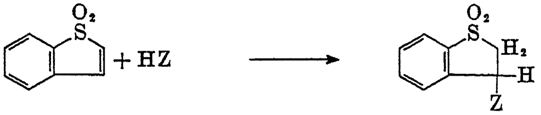
B. Reactions

Thianaphthene 1-dioxide has been shown by two sets of investigators (100,61,62) to react similarly to a vinyl sulfone. It shows none of the aromatic properties of its parent compound, thianaphthene. Bordwell and McKellin (62) considered possible resonance hybrid forms illustrated in eq. 256 as III, IV, and V. III may be looked upon as containing a heteroaromatic system if resonance hydrid forms such as IV and V, in which the outer sulfur orbitol contains ten electrons, are recognized as important. In a chemical sense, carbon-carbon bonds in aromatic systems differ from olefinic bonds in showing less susceptibility to attack by addition-type reactions. When attack by such reagents is successful, a proton is frequently expelled in the course of the reaction to reestablish the aromatic system, the result being substitution rather than addition. In the course of numerous reactions it was found that the 2-3 carbon double bond was almost identical to the double bond in vinyl sulfones, since alcohols, hydrogen, water, amines, halogen acids, and halogens added as illustrated in eq. 257. Z, in the above instance, may be negatively charged ions such as OR, SC_6H_5, OH, Br, NR_2, or $CH(COOC_2H_5)_2$, examples of which are found in Table II-23.



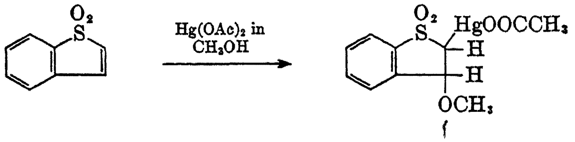
(III) (IV) (V)

(256)



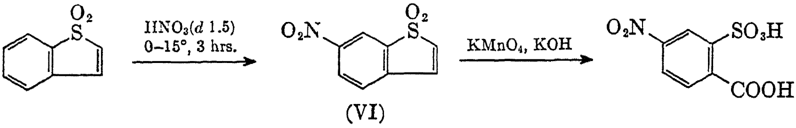
(257)

Methanolic mercuric acetate adds to the double bond to give a compound resembling the addition product of $CH_3OHgOOCCH_3$ (100) (eq. 258). Nitration of thianaphthene 1-dioxide yields 6-nitrothianaphthene 1-dioxide,



(258)

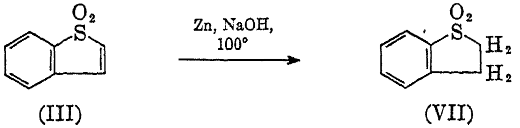
VI (100). Its structure was established by rupture of the thiophene ring to yield 4-nitro-2-sulfobenzoic acid (eq. 259). VI when treated with bromine in glacial acetic acid yields the 2,3-addition product, 6-nitro-2,3-dibromo-2,3-dihydrothianaphthene 1-dioxide (100).



(259)

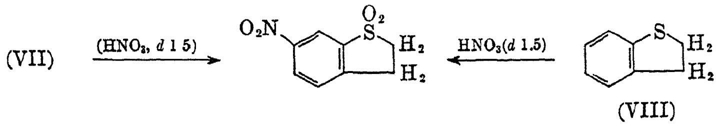
Thianaphthene 1-dioxide has recently been shown to undergo an internal Diels-Alder reaction (733). The resultant dimer loses sulfur dioxide and a dihydronaphtho[2,1-*b*]thianaphthene results (see Chapter VI, section II-F, for further details).

Thianaphthene 1-dioxide (III) is readily reduced to the 2,3-dihydro derivative (VII). Zinc and sodium hydroxide effect this reduction in high yields (100) (eq. 260). Compound VII is obtained in quantitative yield when III is reduced in the Parr hydrogenation apparatus with three atmospheres of hydrogen pressure using 5% palladium on charcoal as catalyst (62). Challenger and Clapham (100) reported that zinc and acetic acid and sodium amalgam and water did not effect this reduction. However, zinc, acetic acid, and hydrochloric acid are reported to reduce III to thianaphthene in 46% yield (722). Lithium aluminum hydride reduces thianaphthene 1-dioxide to 2,3-dihydrothianaphthene (628,722). Compound VII has been prepared by other methods. Fricke and Spilker (193) oxidized 2,3-dihydrothianaphthene with hydrogen peroxide and von Braun (67) oxidized 2,3-dihydrothianaphthene with potassium permanganate. β-Phenylethylsulfonyl chloride undergoes an internal Friedel-Crafts reaction at 40° in the presence of aluminum chloride to yield 37% of VII (738). 3-Oxo-2,3-dihydrothianaphthene 1-dioxide is reduced by hydrazine hydrate via the Wolff-Kishner reaction to give a 92% yield of VII (756). The difficulties involved in preparing 2,3-dihydrothianaphthene and other intermediates would indicate that the method involving hydrogenation of III over palladium (62) is the best method for preparing this compound.



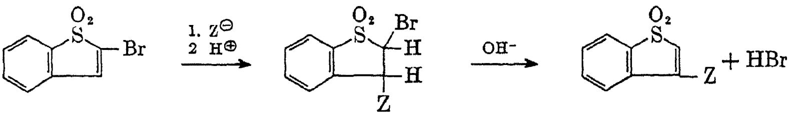
(260)

6-Nitro-2,3-dihydrothianaphthene 1-dioxide is formed by either direct nitration of VII or of 2,3-dihydrothianaphthene, VIII (100,61) (eq. 261).



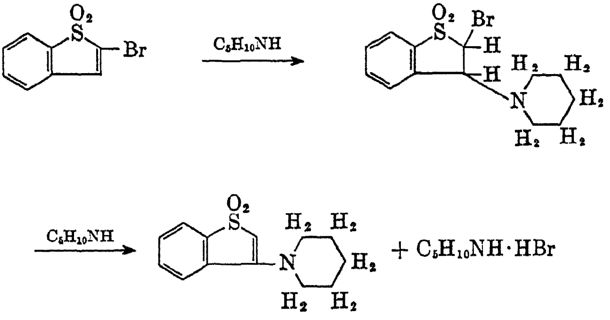
(261)

2-Bromothianaphthene 1-dioxide has been prepared in quantitative yield by dehydrobromination of 2,3-dibromo-2,3-dihydrothianaphthene 1-dioxide with pyridine (61). Attempts to replace the 2-bromo group in this compound yielded only 3-substituted products (61). The reaction probably involves an attack at the 3-position by a nucleophilic negative ion with subsequent addition of a proton at carbon 2 to give an intermediate addition complex, the final 3-Z derivative resulting by dehydrobromination (eq. 262). In the case where HZ is piperidine, an intermediate



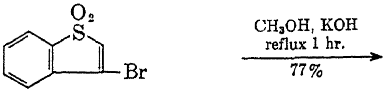
(262)

addition product was isolated when equimolar amounts of piperidine were employed. The final step of the reaction was shown to be a simple dehydrobromination when the intermediate was treated with an additional mole of piperidine (eq. 263).



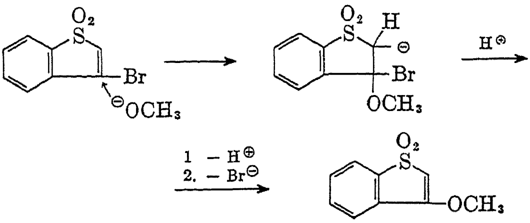
(263)

The bromine atom in 3-bromothianaphthene 1-dioxide is replaced normally and the expected 3-substituted derivatives are obtained. The bromine atom of this compound is replaced much more easily than the bromine atom of 3-bromothianaphthene, since it is replaced by a methoxyl group when refluxed with methanolic potassium hydroxide under typical Williamson ether synthesis conditions (59) (eq. 264). Compound II is

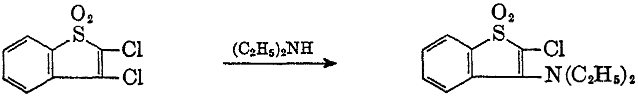


(264)

conveniently split by acid to yield 3-hydroxythianaphthene 1-dioxide. The activity of the 3-bromo group in this reaction is quite comparable to that of the bromo atom in an alkyl bromide. However, considering the olefinic nature of the double bond, addition of methanol at the 2- and 3-carbons is probably the initial step, and II is formed by dehydrobromination of the intermediate (eq. 265). The 2,3-dihalothianaphthene 1-dioxides have been prepared, but the details of the syntheses have not yet been published (540,748). Their physical constants, however, are listed in Table II-23. The 3-halo atom is the most reactive and these compounds react with amines as shown in eq. 266. This reaction was also carried out with morpholine and piperidine with both the 2,3-dichloro- and the 2,3-dibromothianaphthene 1-dioxides. The 3-amino group in the 2-chloro-3-diethylamino derivatives is easily cleaved by acid, and the investigators considered the resultant hydrolysis product to exist in the keto form, which could be chlorinated further to yield 2,2-dichloro-3-oxo-2,3-dihydrothianaphthene 1-dioxide (540,748) (eq. 267).

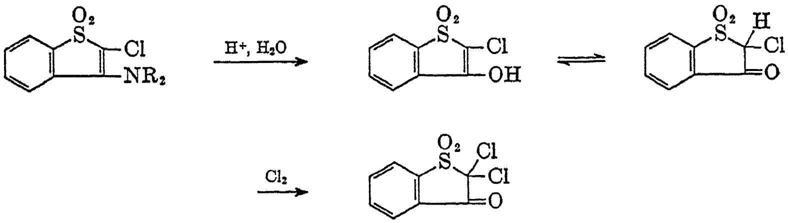


(265)

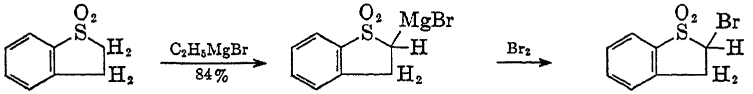


(266)

2-Bromo-2,3-dihydrothianaphthene 1-dioxide is prepared by a novel synthesis which involves reacting 2,3-dihydrothianaphthene 1-dioxide with ethyl magnesium bromide. Subsequent bromination yields 2-bromo-2,3-dihydrothianaphthene 1-dioxide (62) (eq. 268). In this respect, VII



(267)

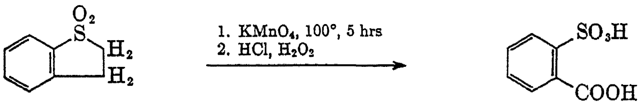


(VII)

(268)

has a hydrogen in the 2-position that appears to be more reactive than the 2-position of thianaphthene itself. It appears likely, therefore, that the 2-sodio derivative of VII could be prepared. This derivative, as well as the possible products from transmetalation with Grignard reagents, should prove an interesting intermediate for further synthesis.

The thiophene ring of 2,3-dihydrothianaphthene 1-dioxide is cleaved by means of the following two-step oxidation (62) (eq. 269). Fricke and Spilker (193) noted that the compound split very readily with chlorine in acetic acid to form *o*-ethylbenzenesulfonyl chloride. This is an interesting reaction in view of the fact that the expected product surely would be *o*-(β-chloroethyl)benzenesulfonyl chloride.



(269)

3a,7a,-Dihydrothianaphthene 1-dioxide is said to form in the Diels-Alder condensation of thiophene sulfone (701). Reactions illustrating the presence of this compound can be found in eq. 285 and in eq. 39A, Chapter VII.

The melting points of the thianaphthene 1-dioxides are listed in Table II-23; Table II-24 is a compilation of the melting points of the 2,3-dihydrothianaphthene 1-dioxides.

TABLE II-23. Melting Points of Thianaphthene 1-Dioxides

Substituent	M.p., °C.	Ref.
None	142–143	342,61,745
5-CH_3	125.5–126.5	504,745
3-C_6H_5	159–161	746
2-Cl	142–143	724

Table continued

TABLE II-23 (*continued*)

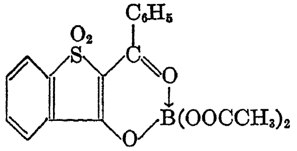
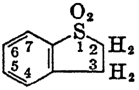
Substituent	M p , °C	Ref
3-Cl	158 5–160	724
	167–168 5	748
2-Br	150–151	61
3-Br	183 5–184	59,60
4-Br	143–144	747
6-Br	139	747
3-I	197–198	P-707
2,3-Cl_2	157–158	540,748
	160–161	724
2,3-I_2	230–231.5	748
2-Cl-2-Br	151–153	748
3-Cl-2-I	188–189	748
3-OH	133	59,748,527
	136–137	14,181
	139	343
5-OH	152–153 5	747
3-OCH_3	215	16
	220	59,61
3-OC_2H_5	165.5–166.5	724
3-OC_6H_5	137	59
2-Cl-3-OCH_3	152–153	724
2-CH_3-3-OH	Above 300	359
2-CH_3-3-$OOCC_2H_5$	110–111	359
2-*p*-$NO_2C_6H_4$-3-OH	186	415
2-*p*-$NH_2C_6H_4$-3-OH	ca. 180	114
2-*p*-$CH_3CONHC_6H_4$-3-OH	226	114
3-$OOCCH_3$-5-Cl	164	190
2-$COOCH_3$-3-OH	177–180	1
2-$COOC_2H_5$-3-OH	137–138	1,14,16
2-$COOC_2H_5$-3-$OCH_2COOC_2H_5$	121	16
2-$COCH_3$	148–149	724
2-$COCH_3$-3-OH	164	114
2-COC_6H_5-3-OH	188	114
	220 (dec.)	114
3-COOH	218 (dec.)	133
4-NO_2	177–178	747
5-NO_2	166	60
3-Br-5-NO_2	190–191	60
6-NO_2	187–188	100,342
	181–182	747
3-NH_2	211–213	59
3-NH-*n*-C_4H_9	145	59
3-$NHCH_2C_6H_5$	193–194	540,748
3-$N(C_2H_5)_2$	186 5–187	59,61
3-Piperidyl	246 (dec.)	59,61
3-Morpholinyl	222–223	61,540
3-Pyridinium bromide	243 (dec.)	748
3-$N(C_2H_5)_2$-5-NO_2	210	60
3-Piperidyl-5-NO_2	197–198	60
3-$N(C_2H_5)_2$-5-NH_2	194	60
2-Br-3-NHC_4H_9	136	748
2-Br-3-$NHCH_2C_6H_5$	161	748
2-Br-3-cyclohexylamino	184–185	748

TABLE II-23 (*continued*)

Substituent	M.p., °C.	Ref.
2-Cl-3-N$(C_2H_5)_2$	124–125	540
2-Br-3-N$(C_2H_5)_2$	142.5–143	540,748
2-Cl-3-piperidino	130–131	540
2-Br-3-piperidino	153–154	540,748
2-Br-3-morpholino	176.5 (dec.)	748
5-NH_2	178	60
5-$NHCOCH_3$	225–226	747
5-N$(C_2H_5)_2$	B.p. 168–171 (0 5 mm.)	60
5-NH_2-3-Br	233	60
5-NH_2-6-Br	229–231	747
5-NH_2-6-NO_2	286–290 (dec.)	747
5-$NHCOCH_3$-4-NO_2	227 (dec.)	747
5-$NHCOCH_3$-6-NO_2	215–216	747
3-CH_2COOH	268–269 (dec.)	724
2-CH_2CN	209–211	724
3-CH$(COOEt)_2$-2-Cl	145–147	748

TABLE II-24. Melting Points of 2,3-Dihydrothianaphthene 1-Dioxides



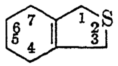
Substituent	M.p., °C.	Ref.
None	91.5–92	62,193,738,756
	98	67
6-CH_3	160.5–161.5	505
2-Br	116–117	62
3-Br	91.5–92 5	62
6-Br	144–145	62
2,3-Br_2	162–165	61
	168–170	342
2,2,3-Br_3	129	748
3-Cl-2,3-Br_2	148 (dec.)	748
2,3-Br_2-6-NO_2	149–150	100
3-I	104–105	100
3-OH	Liquid	62
3-$OOCCH_3$	89.5–90	62
3-$OOCC_6H_5$	107–108	62
3-OCH_3	77–78	100
3-OC_2H_5	108–109	62,100,746
3-OCH$(CH_3)_2$	96–97	62
3-OC$(CH_3)_3$	115–116	62
2-SC_6H_5	123–124	746
2-$SO_2C_6H_5$	147–149	746
2-SC_6H_4-*p*-CH_3	118–120	746
2-SC_6H_{11}	Oil	746
2-$SO_2C_6H_{11}$	80–81	746
2-$SCH_2C_6H_5$	Oil	746
2-$SO_2CH_2C_6H_5$	195–195.5	746

Table continued

TABLE II-24 (*continued*)

Substituent	M.p., °C.	Ref.
3-SC_6H_5	69–70	62
3-$SO_2C_6H_5$	177–178	62
3-$N(C_2H_5)_2$	97.5–98	62
3-Piperidino	109–110	62
3-Morpholino	177 5–178.5	62
2-Cl-3-cyclohexylamino	182–183	748
2-Cl-3-$N(C_2H_5)_2$	124–125	748
2-Cl-3-piperidino	130–131	748
2-Cl-3-morpholino	166 (dec.)	748
2-Br-3-$NHCH_2C_6H_5$	217	748
2-Br-3-$N(C_2H_5)_2$	88–88 5	748
2-Br-3-piperidino	139–140	61,748
2-Br-3-morpholino	156–157	61,748
3-Oxo	133	748,756
2,3-Dioxo	265	410
	220	114
2-Cl-3-oxo	154–155	540,748
2-Br-3-oxo	149–150	114,748
2,2-Cl_2-3-oxo	109–110	540,748
2,2-Br_2-3-oxo	148	114
2,2-I_2-3-oxo	155–157	748
2-Cl-2-Br-3-oxo	125–126	748
3,3′-Dioxo-2,2′-methylene	246	748
3,3′-Dioxo-2,2′-Br_2-2,2′-methylene	268 (dec.)	748
2-*p*-$NH_2C_6H_4$-3-oxo	ca. 180	114
2-*p*-$CH_3CONHC_6H_4$-3-oxo	226	114
2-Br-2-C_6H_5-3-oxo	170	114
2-Br-2-*p*-$NO_2C_6H_4$-3-oxo	155	114
2-Br-2-COC_6H_5-3-oxo	168	114
2-OH-2-*p*-HOC_6H_4-3-oxo	123 (dec.)	114
3-Phenylhydrazone	245–246 (dec.)	360
	249	748
	188–189	756
2-$C(=NNHC_6H_5)C_6H_5$-3-phenylhydrazone	243	114
3-Oxime	245–246	748
3-Oxime (*O*-picryl ester)	195–197 (dec.)	748
3-Oxime (*O*-benzenesulfonyl ester)	166–167	748
3-CH_3O-3-$NHCH_2C_6H_5$	148–150	748
3-CH_3O-3-piperidino	78–80	748
2-Cl-3,3-$(CH_3O)_2$	150–151	748
2-Cl-3,3-$(C_2H_5O)_2$	117–118	748
2,2-Br_2-3,3-$(CH_3O)_2$	188–189	748
3-$CH(COOEt)_2$	84.5–85.5	62
2-$HgOOCCH_3$-3-OCH_3	151–153	100
2-$HgOOCCH_3$-3-OC_2H_5	163–164	748
2-HgOH-3-OC_2H_5	214–215	748
2-HgCl-3-OCH_3	177–179	748
2-HgBr-3-OCH_3	163–164	748

B. Isothianaphthene and Its Derivatives



(*Ring Index* No. 854)

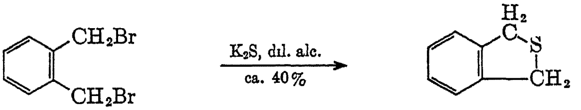
Isothianaphthene
Benzo[*c*]thiophene

Although thianaphthene is a well-known compound, its isomer, isothianaphthene, is unknown. Several possible syntheses are obvious. For example, the ring closure of *o*-xylene by merely heating with sulfur should produce low yields of this compound. Another possible synthesis is the dehydrogenation of the known 1,3-dihydroisothianaphthene. The fully aromatic ring system appears to be stable, since derivatives are reported.

I. The Hydroisothianaphthenes

A. 1,3-Dihydroisothianaphthene (*o*-Xylylene Sulfide)

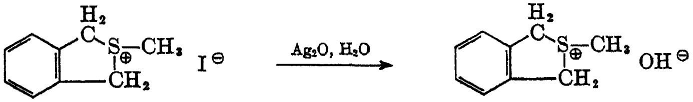
1,3-Dihydroisothianaphthene has been prepared in fair yields from *o*-xylylene dibromide and potassium or sodium sulfide (541,542,296,68) (eq. 270). It also is formed by heating a solution of disodium xylylenedimercaptide in a sealed tube at 120–130° (542).



(270)

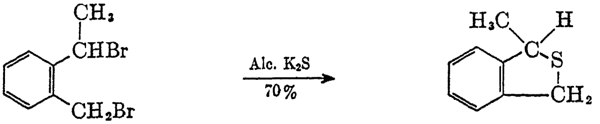
The compound forms a crystalline methiodide (296,68) and an adduct with mercuric chloride containing two moles of 1,3-dihydroisothianaphthene per mole of mercuric chloride (296). It also forms a water-soluble adduct with mercuric acetate (714). The original compound is regenerated with hot hydrochloric acid. It is oxidized to a sulfone, 1,3-dihydroisothianaphthene 2-dioxide, by means of potassium permanganate in dilute sulfuric acid.

The methiodide of 1,3-dihydroisothianaphthene, 2-methyl-1,3-dihydroisothianaphthenyl sulfonium iodide, can be converted by means of silver oxide into the corresponding sulfonium hydroxide (296) (eq. 271). The sulfonium base is said to be crystalline and strongly basic.



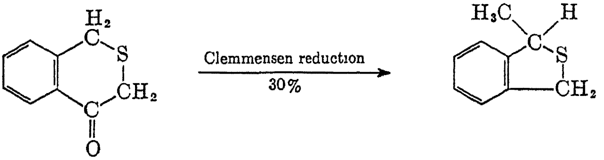
(271)

von Braun and Weissbach (68) have prepared 1-methyl-1,3-dihydroisothianaphthene by the ring closure method of Leser (eq. 272). The



(272)

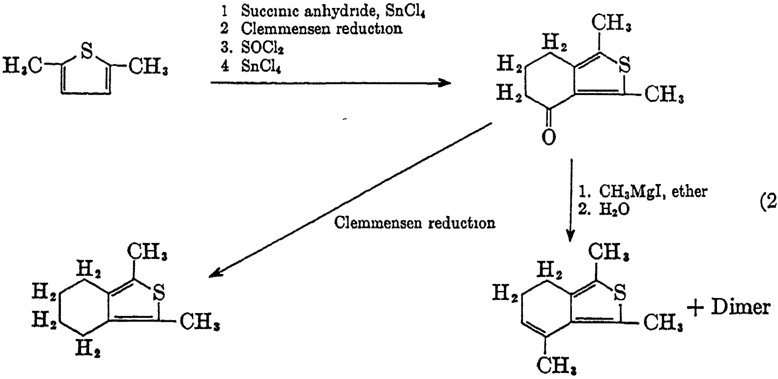
same compound results by a rearrangement of 4-oxobenzoisothiochromane during the Clemmensen reduction (68) (eq. 273).



(273)

B. 6,7-Dihydro- and 4,5,6,7-Tetrahydroisothianaphthenes

The parent compounds of these two series are not known. However, 1,3-dimethyl derivatives have been prepared by the Fieser and Kennelly (184) ring-closure method, using 2,5-dimethylthiophene as the starting material (482,624). The overall yield of products from the sequence of reactions of eq. 274 is not reported, but it appears to be satisfactory.



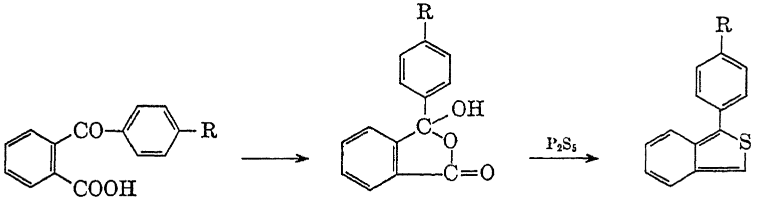
(274)

II. Derivatives of Isothianaphthene

The only known homolog of isothianaphthene is the 1,3,4-trimethyl derivative. This has been prepared by the dehydrogenation of 1,3,4-

trimethyl-6,7-dihydroisothianaphthene (see eq. 274) with selenium (624). The yield was not reported.

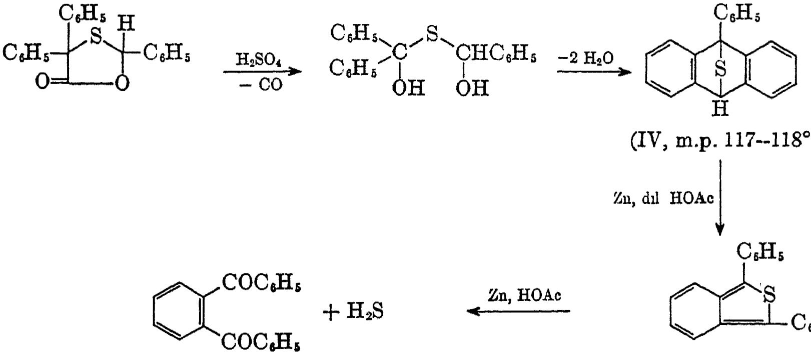
o-Benzoylbenzoic acid and its derivatives form hemiacetals which, when reacted with phosphorus pentasulfide, are reported to yield 1-arylisothianaphthenes (400) (eq. 275). Compound I, where R is H, reacts with solid sodium hydroxide at 340–350° to give a test for divalent sulfur. This indicates rupture of the thiophene ring. Compound I is inert to copper powder in diphenyl at 255–265°. Sodium metal or mercuric oxide failed to react with I. The indophenine test with isatin and sulfuric acid was negative. Oxidation yielded an unknown yellow compound melting at 186° (400).



(275)

(I)
R = H, CH_3, or Cl

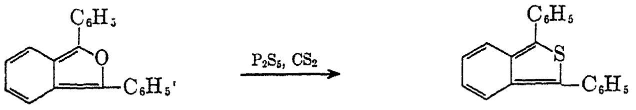
1,3-Diphenylisothianaphthene has been synthesized by a multiple-step reaction from the lactone of α-hydroxybenzylthiobenzilic acid (88) in the following fashion. The structure of the resultant product V was established by reductive rupture of the thiophene ring with zinc and acetic acid (eq. 276). Later investigators (151) verified this work and gave additional proof of structure by obtaining V from 1,3-diphenylisobenzofuran and phosphorus pentasulfide (eq. 277). Zinc amalgam is reported to reduce



(IV, m.p. 117–118°)

(276)

(V)

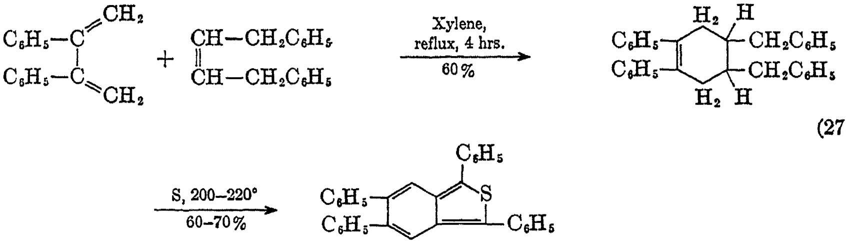

(V)

(277)

V to *o*-dibenzylbenzene (709). Pyrolysis of V with zinc at 400° gives the known 9-phenylanthracene. Both *o*-dibenzoylbenzene and 1,3-diphenylisobenzofuran over zinc dust at 400° yield 9-phenylanthracene (151).

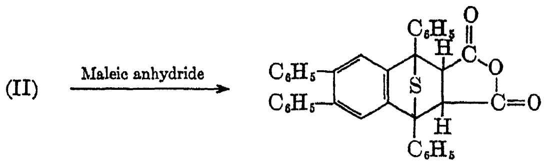
1-Phenyl-3-*p*-tolylisothianaphthene, 1-phenyl-3-*p*-chlorophenylisothianaphthene, 1-phenyl-3-*m*-chlorophenylisothianaphthene and 1-phenyl-3-*m*-nitrophenylisothianaphthene have also been prepared through the synthesis described in eq. 277 (50).

1,3,5,6-Tetraphenylisothianaphthene has been synthesized by the sequence of reactions of eq. 278 (3). Compound II does not add methyl


(II)

(278)

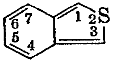
iodide. When oxidized with chromic oxide or nitric acid, 4,5-diphenyl-1,2-dibenzoylbenzene results. Compound II reacts with maleic anhydride to give a product designated as 1,4,6,7-tetraphenyl-1,4-thio-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic acid anhydride, m.p. 245° (dec.), by the investigators (3) (eq. 279). Compound III dissociates at its melting


(III)

(279)

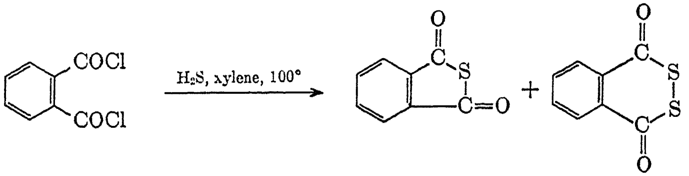
point into its components. It does not add *p*-$CH_3C_6H_4SO_3CH_3$ at 200°, nor does it add methyl iodide. III is converted to 1,4,6,7-tetraphenylnaphthalene-2,3-dicarboxylic acid with alcoholic hydrogen chloride through the loss of hydrogen sulfide.

TABLE II-25. The Isothianaphthenes



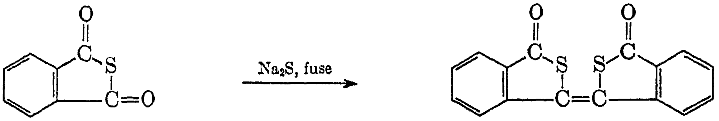
Substituent	B.p., °C. (mm.)	M.p., °C.	Deriv.	M.p., °C.	Ref.
1,3-Dihydro	108 (14) d_4^{26} 1.143	26	Methiodide 2-Dioxide	175 150–152	67,296,542
1,3-Dihydro-1-CH_3	115–116 (16)	—	Methiodide $HgCl_2$ complex	137 121	68
1,3-Dihydro-1,1,3-triphenyl	—	—	Sulfone	—	704
6,7-Dihydro-1,3,4-tri-CH_3	135–140 (15)	—	—	—	624
1,3-Di-CH_3-4,5,6,7-tetrahydro	245 (760)	—	—	—	482
1,3-Di-CH_3-4-oxo-4,5,6,7-tetrahydro	152–153 (13)	46 (39.5–41)	—	—	482,624
1,3-Dioxo	—	113–114	—	—	645,96,499
1,3,4-Tri-CH_3	148–153 (15)	—	Picrate	Brown	624
1-C_6H_5	—	236–237	—	—	400
1-*p*-$CH_3C_6H_4$	—	217	—	—	400
1-*p*-ClC_6H_4	—	241–242	—	—	400
1,3-Di-C_6H_5	—	118–119 (106 5–107 5)	—	—	151 (88)
1-C_6H_5-3-*p*-$CH_3C_6H_4$	—	103–104	—	—	50
1,3,5,6-Tetra-C_6H_5	—	227–228	—	—	3

Isothianaphthene-1,3-dione (thiophthalic anhydride) has been prepared, but the stability of this highly strained thiophene ring has not been studied. Presumably it would not be appreciably more stable than the corresponding furanoid ring in phthalic anhydride. This compound can be prepared from the action of hydrogen sulfide on phthaloyl chloride in xylene at 100° (499) or by condensation of phthaloyl chloride with potassium sulfide (96) (eq. 280). This compound is also said to be formed in 68.5% yield by heating sodium sulfide and phthalic anhydride (645).



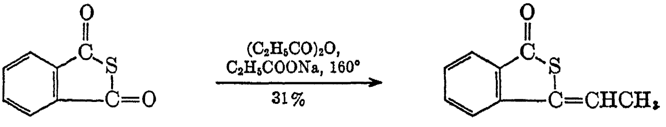
(280)

Hydrogen peroxide in dilute methanol converts this material to methyl phthalate (317). Fusion with sodium sulfide gives a low yield of a compound said to have the structure of VI (eq. 281). When heated with sodium propionate in the presence of propionic anhydride, the 3-ethylidene derivative is formed (646) (eq. 282).



(281)

(VI)
Yellow, m.p. 335°

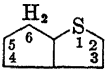


(282)

m.p. 56–57°

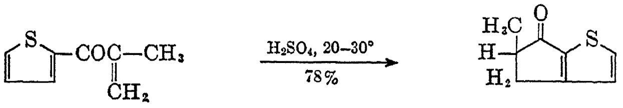
C. Miscellaneous Systems

I. Cyclopenta[*b*]thiophene



6*H*-Cyclopenta[*b*]thiophene

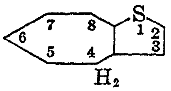
The parent compound of this series is unknown. Burckhalter and Sam (729) have prepared the 5-methyl-6-oxo-4,5-dihydro derivative by cyclization of 2-thienyl 2-isopropenyl ketone with sulfuric acid (eq. 283). A



(283)

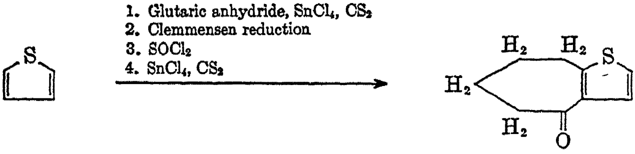
2,4-dinitrophenylhydrazone derivative melts at 248°. The compound has the following physical constants: b.p. 95.5° (2 mm.); n_D^{20} 1.5808; d_{20}^{20} 1.1890; M_D 42.48 (41.80 calcd.)

II. Cyclohepta[*b*]thiophene



4*H*-Cyclohepta[*b*]thiophene

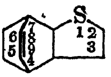
In this miscellaneous class only one compound, 4,5,6,7,8-pentahydrocyclohepta[*b*]thiophen-4-one, is known. It has been synthesized by the well-known Fieser and Kennelly ring closure (184) employing thiophene and glutaric anhydride (89) (eq. 284). The compound was reported to



(284)

boil at 145° at 17 mm., to melt at 31–32°, and to form a semicarbazone, m.p. 208°. No other reactions with this compound were reported.

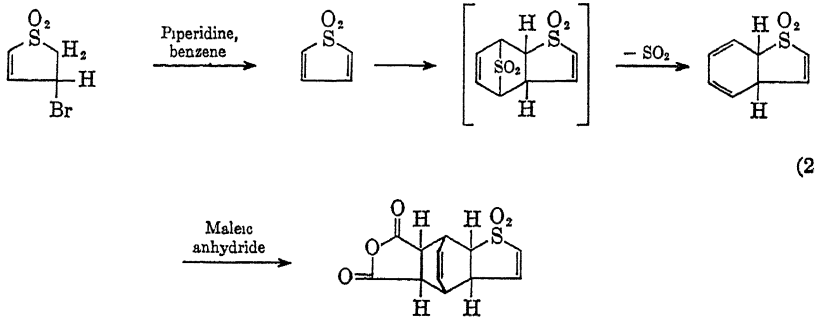
III. 4,7-Endovinylenethianaphthene



4,7-Endovinylenethianaphthene

This system is known only in the form of the sulfone of hydro derivatives. It has been prepared from a complex two-step Diels-Alder reaction

(701). The unstable 3a,7a-dihydrothianaphthene 1-dioxide is indicated as the intermediate that reacts with maleic anhydride (eq. 285). The adduct melts at 305–306°. It forms a dimethyl ester melting at 228.5–229.5°.



(285)

CHAPTER III

Thioindigo and Related Dyes

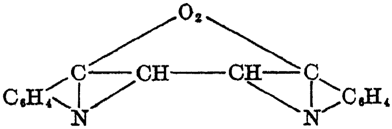
Introduction

The isosteric relationship between indigo and thioindigo dyes was responsible for the rapidity with which the thioindigo dyes reached commercial importance almost immediately after the announcement of the original syntheses by Paul Friedländer in 1906. The chemistry of the indigos was so well established then that very little time was needed to develop the thioindigos commercially.

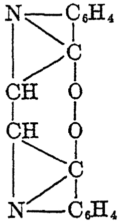
The origin of indigo appears to be as old as the art of dyeing, which is buried in the folds of antiquity. It actually appears to have been discovered in the same relative era as the development of the weaving of animal and vegetable fibers into cloth. Many vegetable and mineral dyes were developed through the ages by the ancient artisans to add color to the drab existence of man. Foremost and most valuable among these were the indigos, the blue and "royal purple" dyes of the kings and emperors.

The indigos are found in nature in two forms. Indigo is obtained from a plant glucoside (indican) from plants grown chiefly in India (the name *indigo* is derived from this source). By fermentation of the glucoside, 3-hydroxyindole (indoxyl) is obtained and this is subsequently converted by air or mild oxidizing agents to indigo. 6,6′-Dibromoindigo, known to the ancients as "Imperial Purple," "Royal Purple," or "Tyrian Purple," was extracted from a species of Mediterranean shellfish.

Little or no chemical information concerning the indigos was reported before 1841, when Erdmann and Laurent isolated a substance they called *isatin* from oxidized indigo. Later, during the period of 1865–1868, Adolph von Baeyer established the structure of isatin and synthesized oxindole. He assigned structures to indigo at that time which are interesting enough to reproduce here.

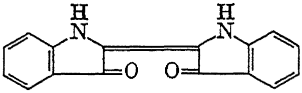


The "Umbrella" Formula



The "Tower" Formula

These erroneous interpretations were modified by Baeyer in 1883 when the proper structure of indigo was published.



The formula used at present is the *trans* form rather than the *cis* form shown above.

During the next score of years Baeyer and his associates carried out intensive research in this field, and the art built up during previous centuries became an exact science. During the same period, Baeyer's students, such as Perkin, Graebe, Gattermann, and many others, were helping to found the modern coal tar dye industry.

Concurrent with development of knowledge of the structure and synthesis of indigo, attempts were being made throughout Europe to substitute the —NH— moiety in indigo by the oxygen atom and other groups such as the carbonyl group which were recognized chromophoric groups in that period.

It is an interesting sidelight that Baeyer discovered "indophenine" and "bromoindophenine" during the period of 1880–1882. At that time, thiophene had not yet been discovered by Victor Meyer, and Baeyer assumed that the dye was a reaction product of isatin and benzene. (It was later shown by Victor Meyer to be a condensation product of thiophene and isatin.) The analysis of Baeyer's indophenine was made by one of Baeyer's students, Paul Friedländer, and quite amazingly these analyses of carbon, hydrogen, nitrogen, and oxygen (by difference) added to approximately 100%. Subsequent analyses by Victor Meyer's students after the dye was shown to form from thiophene and isatin indicated the presence of 15% sulfur which mysteriously was covered by the percentages of carbon and hydrogen in the original analysis.

Although Friedländer made this rather inauspicious beginning in thiophene dye chemistry, it was he who first synthesized 3-hydroxythianaphthene and oxidized it to the first synthetic thioindigo dye, which subsequently laid the foundation for the thioindigo dye industry. The continued importance of this series of dyes in modern dye technology is shown in the latest reported figures of the U. S. Tariff Commission, "Synthetic Organic Chemicals, U. S. Production and Sales 1948," which estimates that 2.5 million pounds of thioindigoid dyes were sold in 1948 at an average selling price of $1.28/lb.

Because of the commercial interest in these compounds, the literature concerning them is quite voluminous. So many thousand dye compositions have been prepared and reported in the literature that it would be prohibitive, from the standpoint of space, to describe them in detail in this chapter. It has been possible to handle only the majority of the articles on this subject in the scientific and trade journals. Those references not employed are listed at the end of the chapter. For the sake of presenting a complete bibliography of the patent literature, Mr. A. J. Johnson of the Jackson Laboratories, E. I. du Pont de Nemours and Company, has kindly consented to present a patent bibliography from his company's files.

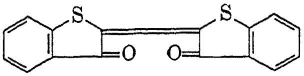
Compilation and tabulation of the physical properties of all the thioindigo dyes and their *leuco* bases, as has been done for the derivatives of classes of compounds in the prior chapters of this book, is not warranted. The more important methods of preparation are represented in an outline form and are generally not referenced. For the most part, publications of Friedländer (46, 47, 182, 195–213) contain the basic methods. The equations are based on the thianaphthene series of compounds only, although the dyes based on the naphthothiophenes and other multiple ring systems are prepared by the same reactions and also have achieved commercial importance. In these cases, the preparation of the intermediate hydroxyl derivatives will be illustrated under the corresponding ring systems of Chapters IV, V, and VI. The dyes of this class of compounds, which were of enough importance at one time or another to be produced commercially, are tabulated along with their trade names and physical properties.

The discussions in this chapter are more from an academic viewpoint than from the practical side with little attention being given to the important industrial dyes and important syntheses. This has been done deliberately, since the most important thioindigo dyes and their syntheses are described adequately in a chapter on indigoid dyes by A. J. Johnson and H. A. Lubs in Lubs, *Chemistry of Synthetic Organic Dyes*, Reinhold Publishing Co., New York, in press.

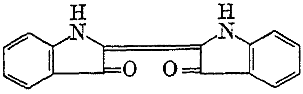
Indophenine and related dyes are included in this chapter. Although the indophenine dyes are not considered to be condensed ring thiophene systems, their close relation to thioindigo dyes makes their inclusion in this chapter more desirable than in *Thiophene and Its Derivatives* (700).

I. Nomenclature

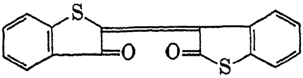
The trivial names attached for the past century to the indigo dyes of the indole series have been transposed into the corresponding thianaphthene series. Thus, thioindigo (I) has been derived from indigo (II) and thioindirubin (III) from indirubin (IV).



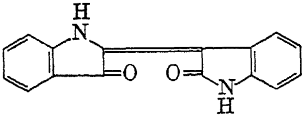
(I)
Thioindigo
2,2′-Bisthioindigo



(II)
Indigo

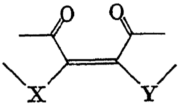


(III)
Thioindirubin
2,3′-Bisthioindigo

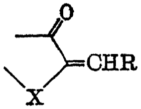


(IV)
Indirubin

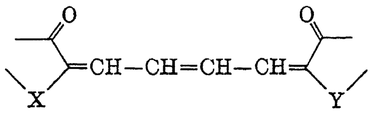
Friedländer (196) suggested that the chromophoric group:



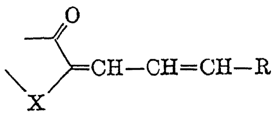
(where *X* and *Y* may be selected from the group of oxygen, sulfur, nitrogen, or carbon) be classified as the *indigoidal* group. Subsequently, he suggested that where *X* has its original connotation and *Y* is a $-CH=CH-$ group, the grouping be known as the *indolignone* group (201). Compounds containing the group:



where *X* has its original connotation and R is usually an aryl or substituted aryl group are referred to as *indogenides* (197). Thus, where *X* is sulfur the compounds are *thioindogenides*. The terms *indigoidal* and *indogenides* have been applied, more recently rather loosely, to vinylogous systems such as the following:

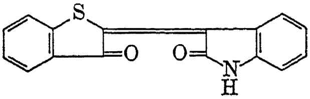


Vinylogous indigoidal group



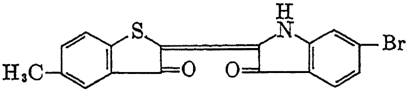
Vinylogous indogenide

The asymmetrical thioindigo dyes are then named on the basis of the *indigoidal* grouping.



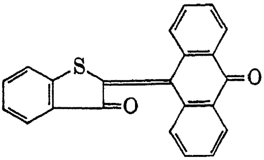
(V)

2-Thianaphthene-3′-indoleindigo
2-Thianaphthene-3′-indoleindirubin



5-Methyl-2-thianaphthene-6′-bromo-2′-indoleindigo

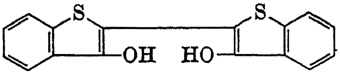
A dye composition derived from anthrol and 2,2-dibromo-3-hydroxythianaphthene (VII) can be classified as vinylogous indolignone (201), but is usually referred to as an indigo.



(VII)

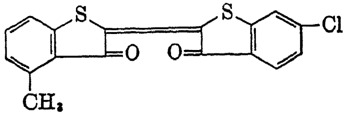
2-Thianaphthene-9′-anthroneindigo
2-Thianaphthene-9′-anthracene indolignone

The leuco forms of these dyes are referred to as *dihydrothioindigos*, *thioindigo whites*, or simply as leucothioindigo or leucothioindirubin, etc.

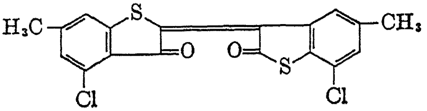


Dihydrothioindigo
Thioindigo white
Leucothioindigo

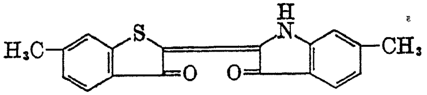
When substituents are on one or more of the benzenoid rings of the indigo dyes, the nomenclature is as follows.



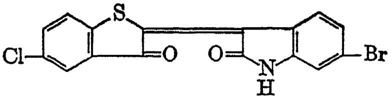
4-Methyl-6′-chlorothioindigo
4-Methyl-6′-chloro-bis-2,2′-thioindigo



4,7′-Dichloro-6,5′-dimethyl-bis-2,3′-thioindigo
4,7′-Dichloro-6,5′-dimethylthioindirubin

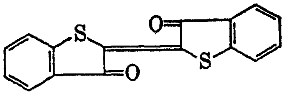


6-Methyl-2-thianaphthene-6-methyl-2-indoleindigo



5-Chloro-2-thianaphthene-6′-bromo-3′-indoleindigo
5-Chloro-2-thianaphthene-6′-bromoindoleindirubin

The configuration of thioindigo dyes was given only a cursory consideration by early investigators. Since indigo had been shown to exist in the *trans* configuration, it was assumed that thioindigo also existed in this form. Recently, investigators at the National Bureau of Standards (633) reported that evidence from absorption spectra indicates that thioindigo dyes exist essentially in the *trans* configuration (VIII):

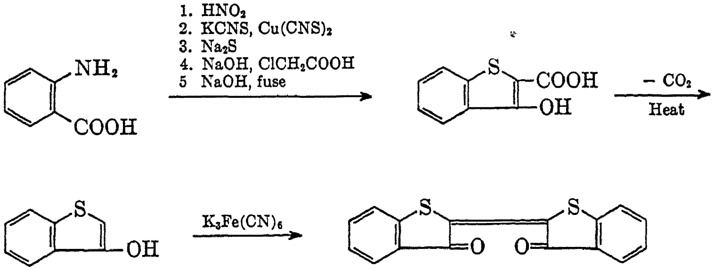


(VIII)

For convenience, most of the formulas in this volume are represented in the *cis* configuration.

II. Friedlander's Commercial Thioindigo Synthesis

The first synthesis of the sulfur analog of *indigo blue* was reported by Friedländer (195) in 1906. This compound was synthesized from a multiple-step reaction involving anthranilic acid as the starting material, and finally the red dye was prepared by a mild oxidation of 3-hydroxythianaphthene (eq. 1).



Thioindigo

(1)

Friedländer was thus able to produce a new, relatively stable red dye by substituting a sulfur atom for the —NH— grouping. Since anthranilic acid was a relatively inexpensive reagent, this reaction was commercially feasible and Kalle and Company, followed quickly by Farbwerke (vorm. Meister, Lucius and Bruning), and Ciba, produced this dye and various other modifications. Table III-1 lists these compounds along with their trade names. The voluminous patent literature during the period of 1906–1912 emphasized processes, methods of manufacture, and manufacture of intermediates. Later in the early 1920's the primary emphasis was on methods of stabilizing the leuco form as the sulfonic acid esters. A complete patent bibliography is given at the end of this chapter.

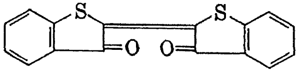
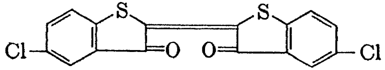
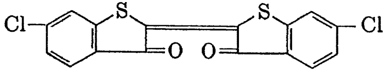
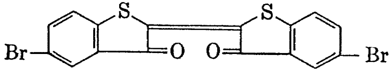
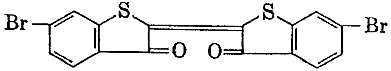
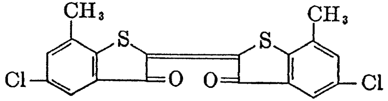
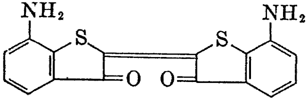
III. Symmetrical Thioindigo Dyes

A. 2,2′-Bisthioindigos

Members of this class of thioindigo dyes are produced by the classical Friedländer synthesis (195) by oxidation of 3-hydroxythianaphthenes with mild oxidizing agents such as potassium ferricyanide (18, 195, 167, 433, 530), ferric chloride (P-276, P-292, P-293), air (213), sulfur monochloride (109), borax (36), hydrogen peroxide (343), or 82% chlorosulfonic acid (416,424).

Another more widely practiced synthesis requires condensation of the anil of 3-hydroxythianaphthene with 3-hydroxythianaphthene (eq. 2)

TABLE III-1. Commercial Thioindigo Dyes (571)[a]

	Trade name	Manu-facturer	Color in concd. H_2SO_4	Color on cotton from hydrosulfite vat	C.I. No.
	Thioindigo Red B Vat Red B Ciba Pink B	K BDC Ciba	Green	Bluish-red	1207
	Thioindigo Red BG Helindon Red B	K MLB	Yellowish-green	Yellow-olive	1209
	Ciba Red B	Ciba	Green	Bluish-red	1210
	Ciba Bordeaux B	Ciba	Yellowish-green	Bordeaux red	1208
	Thioindigo Pink BN, AN Helindon BN	K MLB	Greenish-blue	Pink	1211
	Thioindigo Red 3B Helindon Red 3B Indanthrene Red Violet RH	K MLB I.G.	Green-olive	Yellow-olive	
	Thioindigo Gray 2B Helindon Gray 2B Indanthrene Gray 6B	K MLB I.G.	Blue-violet	Silver-gray	1213

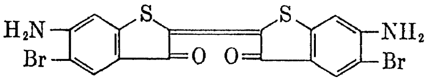
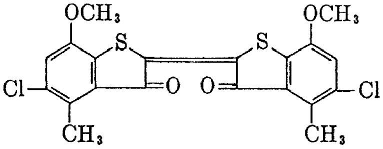
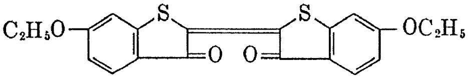
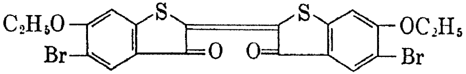
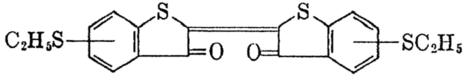
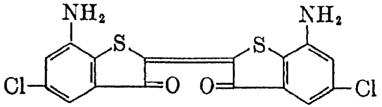
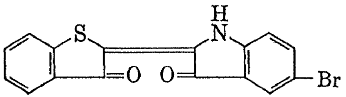
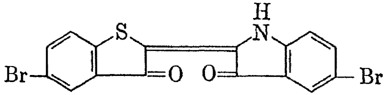
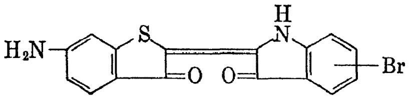
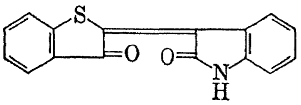
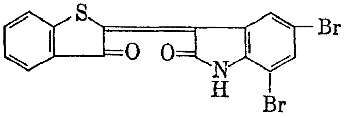
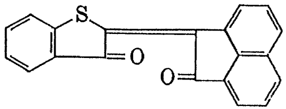
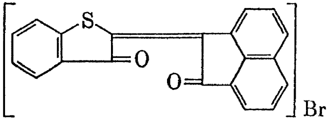
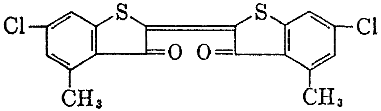
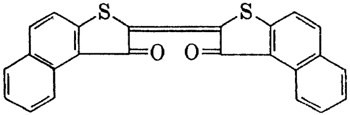
	Trade name	Manu-facturer	Color in concd. H_2SO_4	Color on cotton from hydrosulfite vat	C.I No.
	Helindon Orange DTg	MLB	Cornflower-blue	Orange	1215
	Helindon Violet BB Helindon Violet B Helindon Violet R Thioindigo Violet 2B	MLB MLB MLB K	Green	Bluish-violet	1219
	Thioindigo Orange R Helindon Orange RTg Algol Orange RF	K MLB I.G.	Red-blue	Orange	1217
	Helindon Pure Scarlet R	MLB	Cornflower-blue	Scarlet	1218
	Thioindigo Scarlet S Helindon Scarlet S	K MLB	Blue-green	Scarlet-red	1216
	Helindon Gray BR	MLB	Blue	Gray	1214
	Ciba Gray G Ciba Gray B	Ciba Ciba	Green	Gray	1220

Table continued

TABLE III-1 (*continued*)

	Trade name	Manufacturer	Color in concd. H_2SO_4	Color on cotton from hydrosulfite vat	C.I. No.
	Thioindigo Violet K	K	Blue-green	Bluish-violet	1221
	Ciba Violet 3B	Ciba			
Tribromo-2-thianaphthene-2-indoleindigo	Ciba Violet B	Ciba	Green	Violet	1222
	Thioindigo Brown 3R	K			
	Helindon Brown 5R	MLB	Blue-green	Brown	1224
Tribromo-6-amino-2-thianaphthene-2-indoleindigo	Thioindigo Brown G	K	Fuchsin red	Brown	1227
	Helindon Brown G	MLB			
Brominated amino-2-thianaphthene-2-indoleindigo	Helindon Brown RR	MLB	Dark violet	Brown	1223
	Thioindigo Brown R	K			
	Thioindigo Scarlet R	K	Brown	Scarlet red	1225
	Durindon Scarlet R	BDC			
	Ciba Red G	Ciba	Olive-brown	Red	1226
	Thioindigo Scarlet G	K			
	Durindon Red Y	BDC			

	Trade name	Manufacturer	Color in concd H_2SO_4	Color on cotton from hydrosulfite vat	C.I. No
	Ciba Scarlet G Thioindigo Scarlet 2B Helindon Fast Scarlet C	Ciba K MLB	Green	Scarlet red	1228
	Ciba Red R	Ciba	Green	Bordeaux red	1229
Tribromo derivative of 6-amino-2-thianaphtheneacenaphtheneindigo	Ciba Orange G	Ciba	Greenish-blue	Orange	1230
	Helindon Pink R Ex	MLB	Green	Pink	Pr. 109
	Indanthrene Brown RRD	I.G.	Green	Brown	Pr. 121

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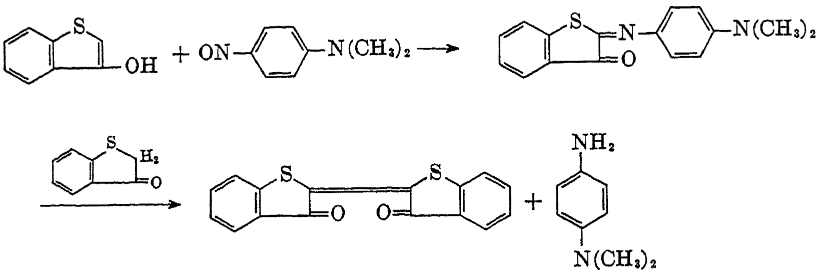
[a] The color index (C.I.) numbers are from F.M. Rowe, ed., *Colour Index*, Society of Dyers and Colourists, Bradford, Yorkshire, 1924, (supplement, 1928). The Pr. numbers indicate Prototype numbers assigned to dyes which have no C.I. numbers; from *Technical Manual and Year Book of the American Association of Textile Chemists and Colorists*, Vol XXV, Howes Publishing Co., 1949.

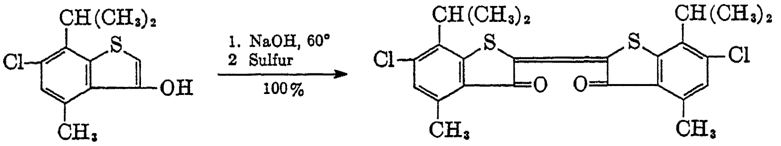
Abbreviations for Manufacturers:

K	Kalle and Co., Aktiengesellschaft, Biebrich a./Rhein.
MLB	Farbwerke vorm. Meister, Lucius und Bruning, Höchst a./Main.
Ciba	Society of Chemical Industry, Basel, Switzerland.
I.G.	I.G. Farbenindustrie A.G.
BDC	British Dyestuffs Corp., England.



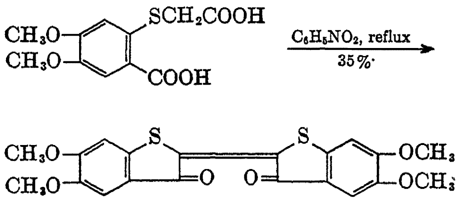
(2)

(see Chapter II). Hixon and Cauwenberg (295) describe the oxidation of 4-methyl-6-chloro-7-isopropyl-3-hydroxythianaphthene with sodium hydroxide and sulfur (eq. 3).

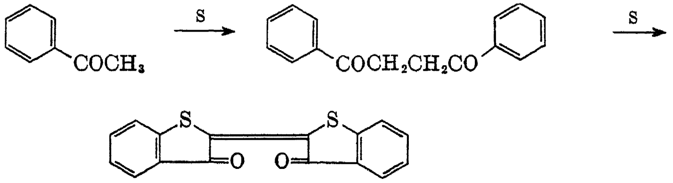


(3)

Certain substituents on the benzenoid ring of 3-hydroxythianaphthene appear to make the methylene group of the keto form of 3-hydroxythianaphthene so reactive that the indigo formation takes place simultaneously with the ring closure in the presence of nitrobenzene (426) (eq. 4).



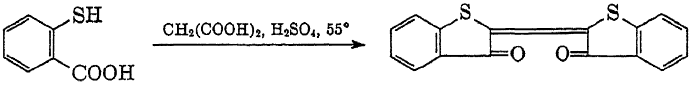
(4)



(5)

Acetophenone when heated with sulfur at 180–210° undergoes a series of reactions yielding thioindigo as the final product (307) (eq. 5). This method of synthesis is also applicable to the *α*- or *β*-acetylnaphthalenes wherein the naphthothioindigos are formed (307,171). A patented process (P-337) describes the condensation of acetophenone and sulfur halides. The resultant product is converted to thioindigo by means of chlorosulfonic acid. A British patent (P-123) uses the same process with α-acetylnaphthalene.

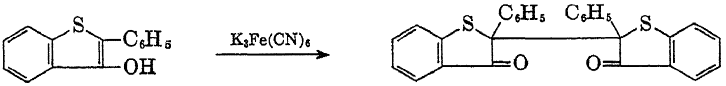
Another direct synthesis of thioindigo involves the interaction of *o*-mercaptobenzoic acid and malonic acid in the presence of sulfuric acid (304) (eq. 6). *o*-Mercaptoacetophenone or acetophenone when treated with sulfur monochloride in the presence of chlorosulfonic acid also yield thioindigo (304).



(6)

Other miscellaneous processes, of the same general character as the two reactions described above, are condensation of 2,2′-dicarboxydiphenyl disulfide with sodium trithiocarbonate (P-411) and internal condensation of $C_6H_5COCH_2SSCH_2COC_6H_5$ by means of aluminum chloride in carbon bisulfide solution (P-393).

If 3-hydroxythianaphthene is substituted in the 2-position by a phenyl group, oxidation yields a colorless compound known as "2,2′-diphenylthioindigo white" (311) rather than an indigo dye (eq. 7). Sunlight also produces the same compound (447). This material on standing or on warming develops a green color which finally changes to brown. The corresponding 2-methyl-3-hydroxythianaphthene (359) or its acetate ester (427) undergoes the same reaction and "2,2′-dimethylthioindigo white" is formed. This is a pale yellow compound melting at 151–153°.



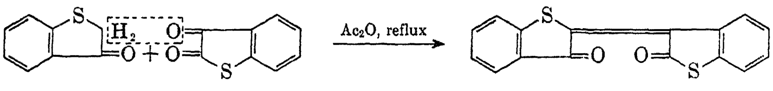
m.p. 236°

(7)

"2,2′-Diphenylthioindigo white" is cleaved by phenylmagnesium bromide. The resultant products are 3-oxo-2-phenyl-2,3-dihydrothianaphthene (75% yield) and biphenyl (719). It also dissociates at 110–130° into free radicals of long life (723,725). When heated in the presence of benzyl alcohol at 130° for two hours, a 70% yield of 3-oxo-2-phenyl-2,3-dihydrothianaphthene and benzaldehyde is obtained.

B. 2,3′-Bisthioindigos (Thioindirubins)

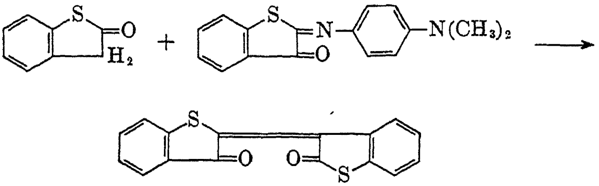
This class of dyes is prepared by condensations of 3-hydroxythianaphthenes in their keto form and 2,3-thianaphthenequinones in the presence



Thioindirubin (8)

of dehydrating agents (199,199a,212) (eq. 8). This synthesis has been shown by Mann and coworkers (282,140,140a) to give mixtures of thioindigos and thioindirubins, depending upon the substituents in the benzenoid ring of the thianaphthenequinone (see details Chapter II).

Marschalk (371) has produced this dye by reacting 2-hydroxythianaphthene (thiooxindole) with the anil of 3-hydroxythianaphthene (eq. 9).



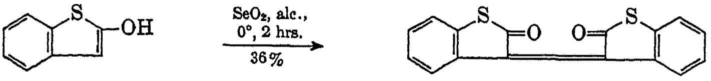
(9)

m.p. 205–207°

The compound was reported to be identical with the thioindirubin prepared by Friedländer (*loc.cit.*).

C. 3,3′-Bisthioindigo (Isothioindigo)

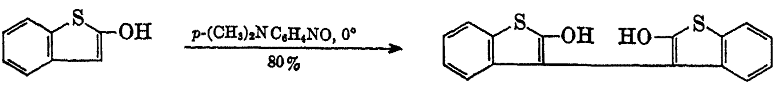
The isomeric 3,3′-thioindigo has been prepared by the action of selenium dioxide on 2-hydroxythianaphthene (110) (eq. 10).



(10)

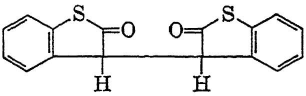
Black-violet
m.p. 224°

An attempt was made by Chovin (110) to convert the 2-hydroxythianaphthene to the corresponding anil derived from *p*-nitrosodimethylaniline, but no condensation took place. Instead the leuco base of 3,3′-thioindigo was obtained (eq. 11). Although the structure of eq. 11 appears likely, the so-called "leucoisothioindigo" appears to be resistant to oxidation and the structure assigned may be incorrect, since the leucothioindigos are



(11)

Leucoisothioindigo
m.p. 260°



readily oxidized by air to the original thioindigo. The investigators proposed the above alternate structure for this compound.

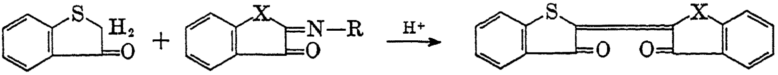
IV. Asymmetrical Thioindigos

This category of thioindigo dyes is the most complex of any of the series of dyes. Foremost among these are the thianaphtheneindoleindigos and dyes of the thioindolignone type such as the acenaphthene series.

These are prepared by the general methods described in section III above and are outlined in the following series of equations.

A. Asymmetrical 2,2′-Thioindogoids

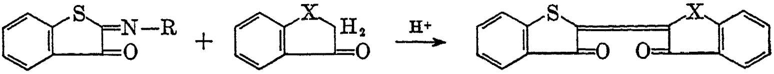
1. Condensation of Thioindoxyl and Anils



(12)

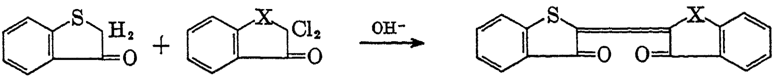
where X is O or NH.

2. Condensation of Anils of Thioindoxyls with Indoxylic Compounds



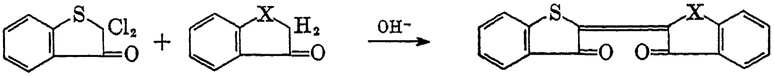
(13)

3. Condensation of Halides of Isatinic Compounds with Thioindoxyl



(14)

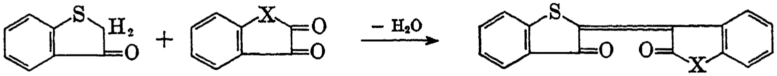
4. Condensation of 2,2-Dihalothioindoxyls with Indoxylic Compounds



(15)

B. Asymmetrical Thioindirubins

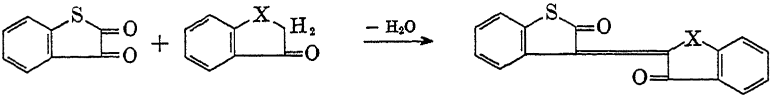
1. Condensation of Thioindoxyl with Isatinic Compounds



(16)

X may also be C=O in this reaction.

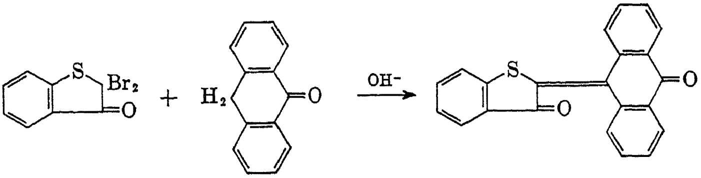
2. Condensation of Thianaphthenequinones with Indoxylic Compounds



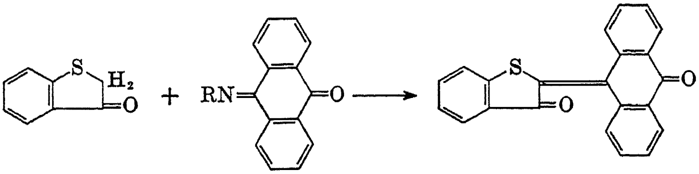
(17)

C. Miscellaneous Thioindigoids and Related Materials

1. Condensation of Dihalides of Thioindoxyl with Anthrol or Anthraquinonemonoanil



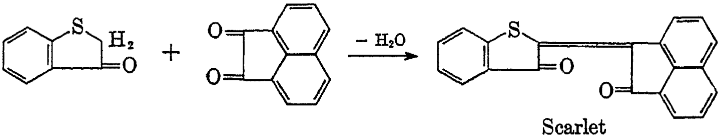
(18)



(19)

2. Condensation of Thioindoxyl with Quinoidal Compounds

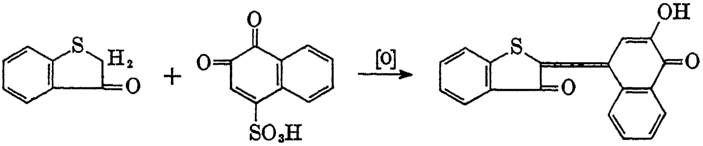
(a) Condensation with Acenaphthenequinone:



(20)

Scarlet

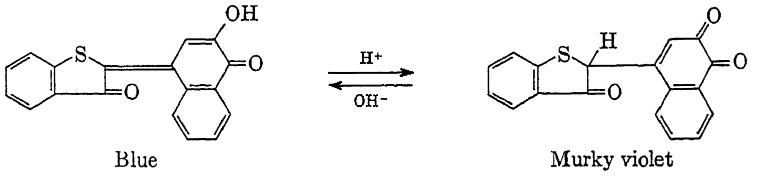
(b) Condensation with Naphthoquinones:



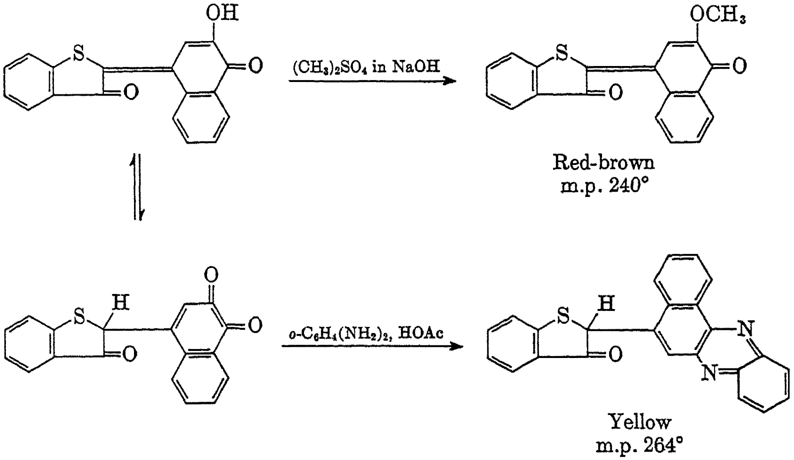
(21)

Red, m.p. 224°

The latter compound was shown by Sachs and Oeholm (436) to exist in two tautomeric modifications (eq. 22). This was established by means of the reactions shown in eq. 23. Additional discussion of this equilibrium is included under *leuco* compounds (section VI).

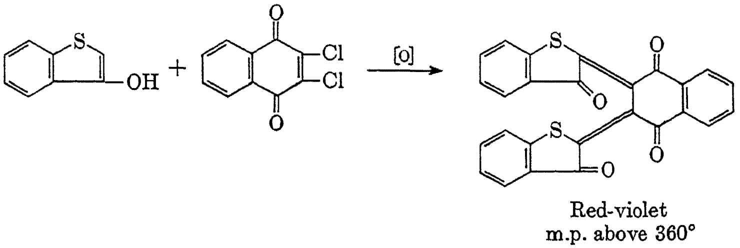


(22)



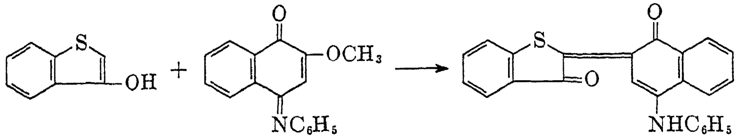
(23)

Another class of indolignones is obtained by reaction of two moles of 3-hydroxythianaphthene with one of 2,3-dichloro-1,4-naphthoquinone



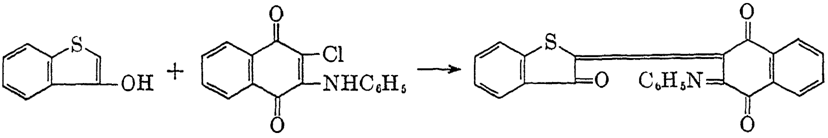
(24)

(218) (eq. 24). With other classes of substituted 1,4-naphthoquinones, the dye compositions of eqs. 25–27 are formed (218).

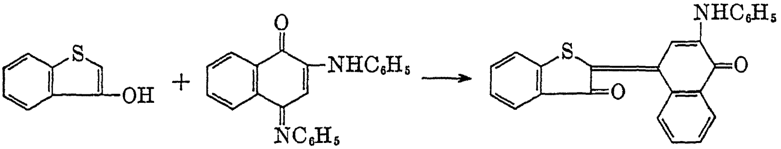


(25)

Blue-green
m.p. 224° (dec.)



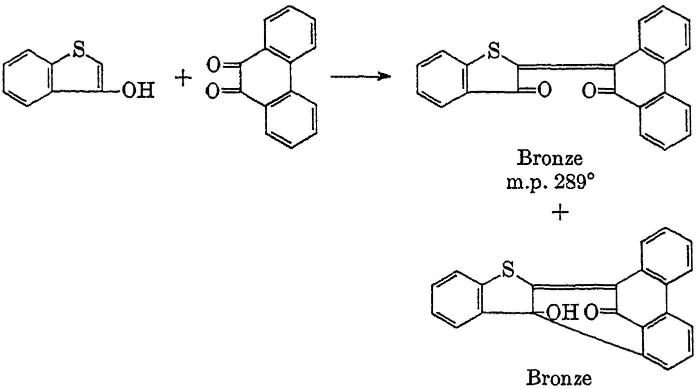
(26)



(27)

D. Condensations with Phenanthroquinones

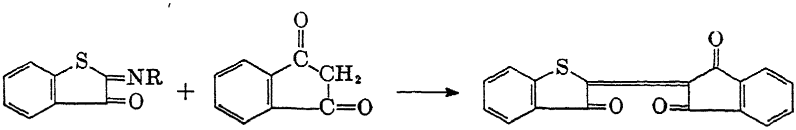
Pummerer and Luther (420) showed that condensation of phenanthroquinone and 3-hydroxythianaphthene yielded two isomers. They postulated that one product was the expected indolignone and that the other isomer was formed by a secondary condensation (eq. 28). The presence



Bronze
m.p. 289°
+
Bronze
m.p. 318°
(28)

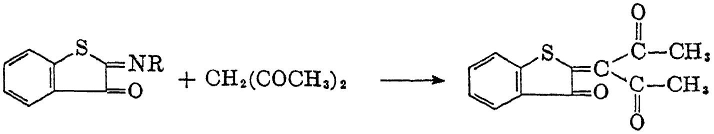
of the hydroxyl group was shown by the formation of an acetate ester. The secondary condensation product is also formed from the indolignone form by boiling in the hydrosulfite vat.

. *Condensation of Anils of 3-Thioindoxyl with Active Methylene Groups*



Red-violet

(29)



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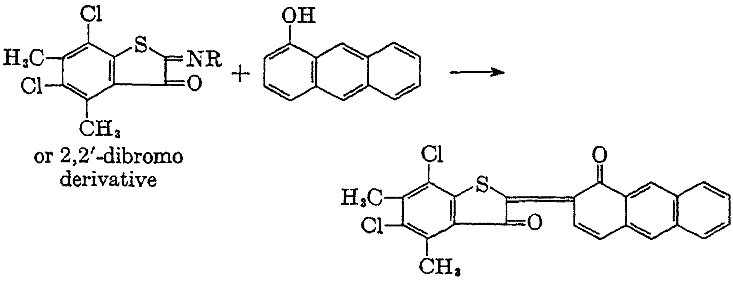
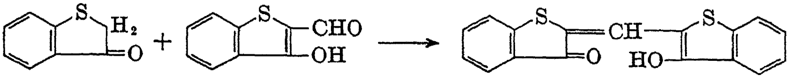


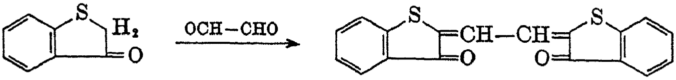
Violet

(31)

2. *Condensations of Thioindoxyl with Aldehydes or Their Anils*



(32)



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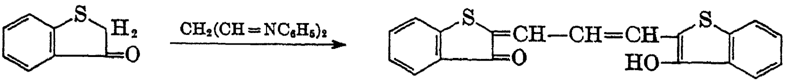

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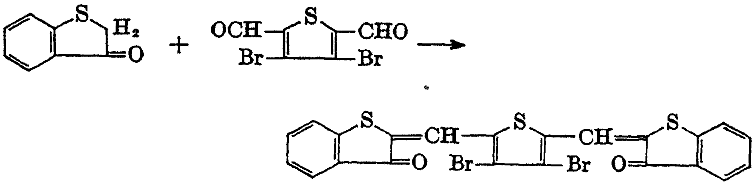
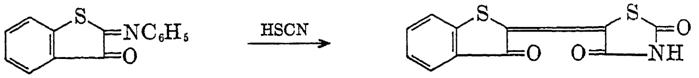


(35)

3. Miscellaneous Condensations



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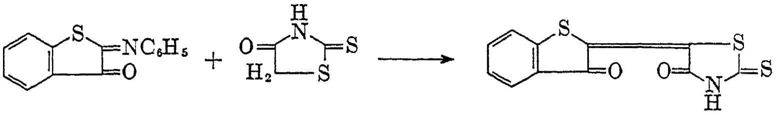

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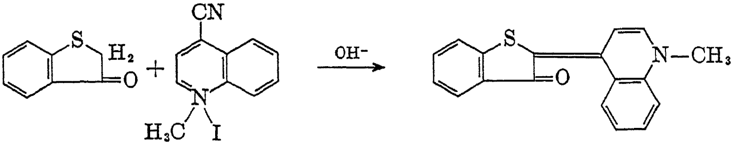

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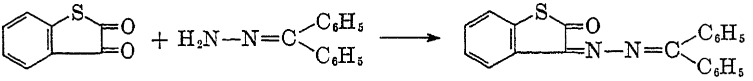

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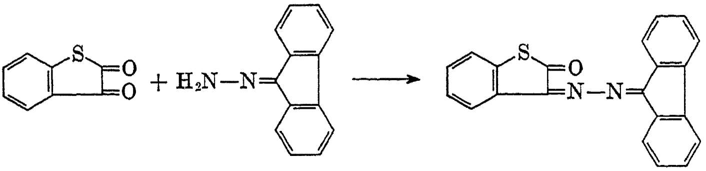


(40)

2,3-Thianaphthenequinone condenses with proline to give a deep green dye composition, $C_{28}H_{17}O_2NS_2$; pyrrole gives a blue composition, $C_{24}H_{14}O_2N_2S_2$; and pyrrolidine a green composition, $C_{24}H_{15}O_2NS$ (249).

V. Thioindogenides and Anils of Thioindoxyls

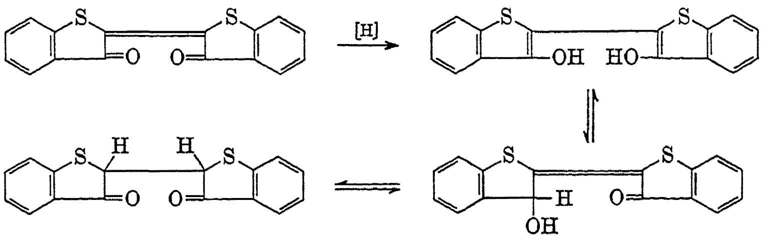
The synthesis of these compounds, which are normally weak dyes, are described in considerable detail in Chapter II. The dyes of this class of compounds have never attained commercial importance.

Thioindogenides form deeply colored complexes with acids and metal salts. For example, the bright yellow 2-piperonylidene-3-hydroxythianaphthene forms black-violet molecular complexes (1:1 ratio) with a wide variety of acids and salts. These compounds are stable to heat below 215° and decompose in water.

VI. Leucothioindigos (Thioindigo Whites)

The reduction of thioindigos with the usual vatting agents such as alkali sulfides or hydrosulfites yields white to faintly colored leuco bases of these dyes. These are soluble in the vat (basic solution) and the cloth to be dyed is dipped into the vat. Air oxidation restores the original color of the dye evenly to the cloth. Among several obvious properties that a successful commercial dye must possess is the ability to form a soluble sodium salt of the leuco base easily and quantitatively, and the leuco base must be quite easily reoxidized by air to the original water-insoluble dye.

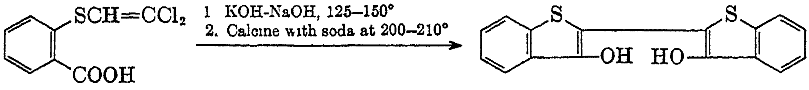
A variety of structures for the reduced form of the thioindigos has been proposed. There appears to be justification for representation of the leuco base in an equilibrium, although the dihydroxy form appears to be the most thoroughly established structure (eq. 41).



(41)

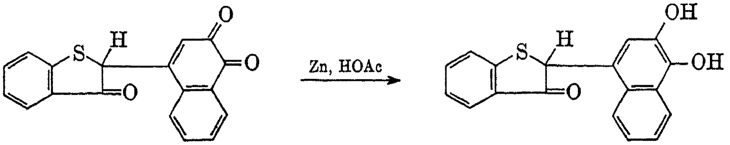
The leucothioindigos form stable esters with acids, and due to their susceptibility to oxidation, are usually stored in this form. Mann and coworkers (282,140,140a,140b) have prepared a series of more than a hundred diacetate esters of leucothioindigos and leucothioindirubins and have described their physical properties and colors. Other pertinent references (37,105,106,107,410,411,551) discuss the preparation, structure, and properties of both mono- and di-esters of leuco bases. The properties of diester-monoamides of the thianaphtheneindoleindigos have also been investigated (411).

The reduction process or the vatting of thioindigo dyes is adequately described in the technical literature on dyestuffs. Among the more recent publications are books by Fox (575) and Diserens (576) and BIOS reports on German industrial production during the war (577,578). The vatting of the thioindigo dyes, in general, follows time-honored procedures for vat dyes. Foremost among these reducing agents are sodium sulfide, sodium bisulfite, sodium hydrosulfite ($Na_2S_2O_4$), formaldehyde-sodium hydrosulfite (a mixture of $NaHSO_3 \cdot CH_2O$ and $NaHSO_2 \cdot CH_2O$), zinc dust, and ferrous sulfate. Hydrazine hydrate has also been used as a reducing agent (63,551). The use of glucose as a reducing agent for Thioindigo S, Thioindigo Scarlet GG and other dyes has been reported (394). Ferrous oxide or a mixture of FeO and Fe in alkaline solution has been patented as a reducing agent for thioindigo and its homologs (P-355). Another patented process (P-497) describes the direct production of leucothioindigo by ring closure of ω-dichlorovinylthiosalicylic acid (eq. 42).



(42)

The structures of the leuco compounds of the thianaphtheneindolignones have not been studied systematically, but Sachs and Oeholm (436) have indicated that reduction of 2-thianaphthene-3-hydroxy-4-oxonaphthaleneindolignone (m.p. 224°) yields the leuco base of the equilibrium structure assigned to the acid form (eq. 43). However, it was not shown

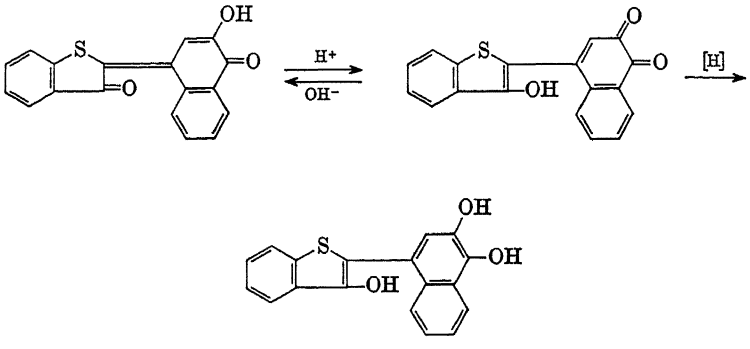


Murky-violet

Leuco compound
m.p. 196°

(43)

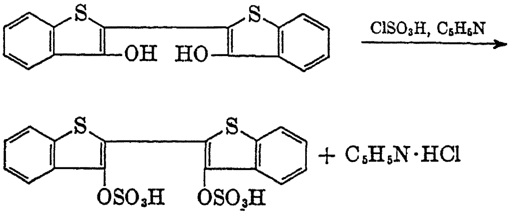
conclusively that the compound did not exist in the trihydroxy form nor was the structure of the acid form of the indolignone established with certainty. It is possible that the proton may shift to the oxygen atom rather than to the carbon atom and that equation 44 more properly represent this equilibrium.



(44)

The sulfuric acid esters of the leuco bases are one of the most important of the dye formulations and have wide applications in the dyeing of wools from the acid bath, and as substantive dyes for cottons. Most commonly they are referred to as *indigosols*, being derived from the original trade name of the products sold by Durand and Hugenin, A.G., who took over the patents of Bader. Later, these esters were sold under the trade names Soledons (Imp. Chem. Ind.), Anthrasoles (I.G. Farbenindustrie), Tinsoles (Geigy), Cibantine (Ciba), and Sandozole (Sandoz).

They are prepared by treating the leuco base with chlorosulfonic acid in pyridine solution by the method of Verley (579) (eq. 45). This method has been adapted and patented by Bader for the leuco thioindigos and by the Scottish Dyes Co., Ltd. Esterification by sulfur trioxide in pyridine is also described as a convenient process (P-106,P-131). The *indigosols* are the disodium salts of the disulfonate esters of this class of compounds. These materials are oxidized to the original dyestuff on the fiber by chromic acid, nitrous acid, or aluminum, sodium, or ammonium chlorate, or ferric chloride.



(45)

VII. Reactions of the Thioindigo Dyes

Thioindigo forms a complex with sodium ethoxide, $C_{16}H_8O_2S_2{\cdot}2NaOC_2H_5$ (338). With sodium amalgam in boiling naphthalene, thioindigo gives a light red composition, $C_{16}H_{10}O_2S_2Na$, from which the original dye is obtained by addition of water (338).

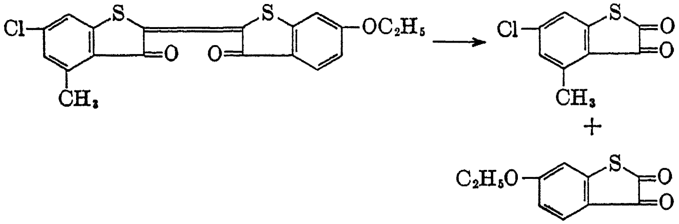
Danaila (143) oxidized thioindigo with nitric acid. The compounds obtained were all red dyes having the following composition and melting characteristics:

I. $C_{16}H_8O_3S$— dec. at 325°
II. $C_{16}H_8O_4S$— dec. at 245°
III. $C_{16}H_8O_5S$— dec. at 237°

Later investigators (410) found that nitrous gases oxidized thioindigo to 2,3-thianaphthenequinone. Other oxidizing agents yield compounds

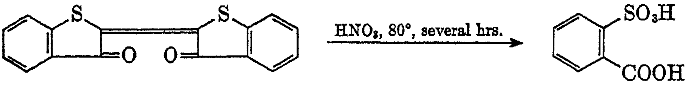
I and II previously found by Danaila. I is described in the later work as being thioindigomonosulfoxide and can be benzoylated in the hydrosulfite vat to give a dibenzoyl derivative of the leuco base; reoxidation yields thioindigo rather than I. Composition II was converted to the 1-dioxide of 2,3-thianaphthenequinone with caustic. II also forms the diacetate of the leuco base when reduced with zinc and acetic anhydride, but is more stable to reducing agents than I.

Ozone cleaves the thioindigo dyes. Fürst and Pollak (225) were successful in identifying both quinones derived from 6-chloro-4-methyl-6′-ethoxythioindigo (eq. 46).



(46)

The thiophene rings of thioindigo can be opened by several methods. A quantitative removal of sulfur is obtained with nickel-aluminum alloy and aqueous sodium hydroxide (627). Predominant quantities of 1,2-dibenzoylethane and 1,4-diphenylbutane along with smaller amounts of benzoic acid have been isolated. 6,6′-Diethoxythioindigo also undergoes this reaction yielding the expected reduction products. Degradation of the thiophene rings occurs when thioindigo is heated with a mixture of fuming and concentrated nitric acid (425) (eq. 47). However, it has been shown that a red dinitro derivative of 6,6′-dichloro-4,4′-dimethylthioindigo (458) can be obtained if the nitration is carried out under carefully controlled conditions with H_2SO_4-KNO_3 at 80–85°. The resultant dinitro derivative, $C_{18}H_{10}O_6Cl_2N_2S_2$, whose constitution was not given, was probably the 5,5′-dinitro derivative.

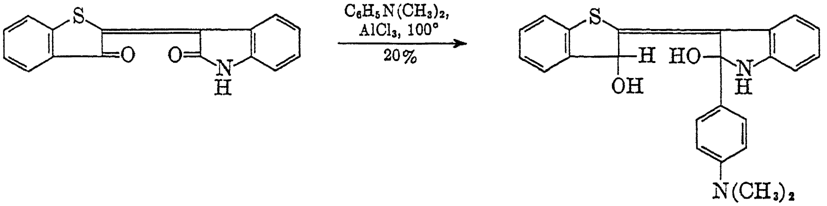


(47)

Thioindigo can be sulfonated directly to give a tetrasulfonic acid derivative, IV (412). The oxidation-reduction potentials of the system IV–leuco-IV were determined for the *p*H range from zero to 11.5. The orange-red oxidant is converted to the yellow reductant by a reaction involving two reduction equivalents per mole. Formation of a deeper red semiquinone was noted in the *p*H region from 8.5 to 11.5.

One of the chief shortcomings of the indigoid dyes is their relatively poor stability to light. This deficiency has been overcome by preparing dyes with halogen substituted in the benzene rings. Although a closer control of shades may be attained by starting with the respective halophenylthioglycolic acids and subsequently obtaining the halothioindigos, commercial practice finds it more desirable to halogenate the finished dye. The halogenation is usually carried out in concentrated sulfuric acid, nitrobenzene, or chlorosulfonic acid. The process is described in detail in the patent literature (P-63,P-64,P-129,P-169,P-279,P-316,P-323,P-329,P-336, P-339,P-542).

Dimethylaniline condenses with 2-thianaphthene-3-indoleindirubin at the 2-position of the indole moiety (551) (eq. 48). Oxidation of V with lead peroxide in ethanol yields a red dye substance, $C_{24}H_{20}O_2N_2S$, m.p. 243 °.



(48)

(V)
m.p. 221°
Diacetyl derivative,
m.p. 205°

The caustic degradation of thioindigo to give the corresponding indole- and thianaphthenealdehydes has been discussed in Chapter II (203,204,-212,312).

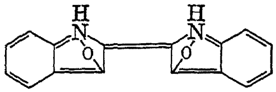
Thioindigo can be determined volumetrically using titanium trichloride as a reductant (320). It also may be determined by electrometric titration employing the cadmium reductor with permanganate or with $^1/_{35}$ *N* ferric chloride or ferric sulfate (510).

2-Thianaphthene-2-naphthaleneindolignone gives a black —$SnCl_3$ derivative with stannic chloride. The pyridine solution is green (366). When the reaction is carried out in dimethylaniline, a dark blue —$SnCl_3$ derivative is formed.

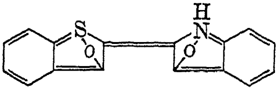
VIII. Factors Affecting the Colors of Thioindigo Dyes

The fact that a definite chromophoric group was responsible for color in dyes was first established by Witt (581). Subsequent theories accounting for the color in certain dyes have been propounded by many investigators, especially Baeyer (582). Claaz (111) and Lifschitz and Lourie (352) have discussed the "indigochromophore" on the basis of their evidence and prior theories.

All of the above theories were based upon the movement of atoms within the molecule rather than upon modern day concepts of resonance. Thus, both Claaz (111) and Lifschitz and Lourie (352) represented the indigo chromophore as an internal oxide.



and

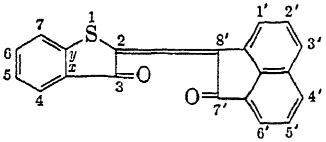


In 1935, Bury (580) restated the principles relating to the structures responsible for the formation of dyes on the modern concept of resonance. Although these principles are more important in the interpretation of other series of dyes than in the thioindigos, it is important that theories appearing in older references be considered from Bury's viewpoint.

It is not the purpose here to discuss fully the effect of benzenoid substituents on the colors of the resultant dyes. In fact, there have been only a few attempts to reduce this vast art to an exact science. Martinet (583) formulated a rule which states that the effects of two auxochromic groups in the para position are cumulative and in the meta position they act in contrary direction (the para and meta positions in the thioindigo dyes are 5 and 5′ and 6 and 6′, respectively). This rule was applied principally for the indigo dyes but Guha (253a to 275 and 780) has made a systematic study on the effect of nonauxochromic groups (CH_3 and Cl) substituted in the benzenoid portion of the molecule and found the rule applied, in general, to the nonauxochromic groups as well. For example, it was found that the 5-methylthianaphthene derivatives of several different series of dyes were more deeply colored than the parent compound of that series, *i.e.*, a bathochromic effect was produced. When substituted in the 4, 6, or 7 position, the methyl group becomes a hypsochrome, i.e., the shades of the parent dye are lightened. Guha (272) summarizes this work in the following statements.

> "It has now been established by the work on thioindigoid dyes that substituents such as CH_3 or Cl, which are not ordinarily regarded as an auxochrome, may have decided influence upon the position and intensity of absorption bonds. The effect of the substituent group may be fairly large but it appears to be the result of displacement or modification of the original curve without introducing any new electronic bond. The influence of these substituents may be regarded as disturbances in existing electronic paths without altering their essential character. A similar example is found in the 2600 A. bond of benzene which is 'allowed' by the cooperation of certain vibrations and is increased by the presence of CH_3, OH, NH_2, or Cl. It may be noted that the wavelength of the absorption maxima under-

goes some noticeable but small change (2680 A. is the highest) from that of the mother compounds, if a CH_3 group is substituted in positions 4, 5, 6, and 7 in the thianaphthene ring. This can be understood by taking into consideration the fact that these positions in the thianaphthene ring are not exactly equivalent with respect to the rest of the molecule. The bond length and the bond strengths are bound to be slightly different in different cases. For example, in the first series, in the molecule of 2-thianaphthene-8′-acenaphthyleneindigo the force between x and the carbon atom in the position 4 to which a CH_3 group is linked will be different from the force between 7 and the carbon at the position 7 to which also one CH_3 group may be attached. This will be so because a CO group is attached to x and one sulfur atom is attached to y. Therefore, the substitution of the CH_3 group in various positions affects differently the vibrations frequency, which is characteristic of the main chromophoric group, —CO—C═C—CO—, being reinforced by the S atom which functions as an auxochrome."



In addition, Guha has shown that the colors of the isomeric methyl thioindigos of the isatin, aceanthrenequinone, and phenanthraquinone series, or the symmetrical thianaphtheneindigos may be arranged in the order 5-Me > parent compound > 4-Me > 6-Me > 7-Me, whereas the color changes in acenaphthenequinone and benzaldehyde series are in the order 5-Me > parent compound > 4-Me > 7-Me > 6-Me.

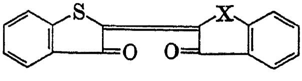
Substituents in the nonthianaphthene portion of the asymmetrical thioindigos and thioindirubins have also been investigated by Guha (272), but no such generalized statements of the effects of these groups have been drawn.

Dutta (153–167) has also made extensive studies of the effect on the color of the thioindigos shown by a fused benzene ring on the benzenoid portion of thianaphthene (*i.e.*, a comparison of the isomeric naphthothiophenes). The color of this series of dyes is usually brown. Conclusions reached in portions of this work (160,166) indicate that the greatest bathochromic effect is produced when the benzenoid substituent has the fused ring in the 5,6-positions. This is true, at least, in the naphthothiophene-9′-phenanthreneindigos, the naphthothiophene-2′-indoleindigos and the naphthothiophene-9′-acenaphthyleneindigos. Thus it appears that deepening of the color in isomers of this class depends on the position at which the new symmetrical ring is added to the thianaphthene nucleus. The effect is greatest when the new ring is so attached that it is equally distant from the two chromophores (S and CO) of the indigo and in such a position that it establishes an equilibrium with the chromophore and auxochrome in the molecule at the same time that it increases the molecular weight.

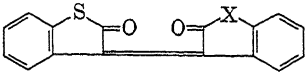
The effect of halogen atoms on the shades of thioindigo dyes is quite pronounced, as can be seen from the list of commercial dyes in Table III-1. No general conclusions can be drawn as to their effects when substituted in definite positions on the benzene ring except that it may be said that, in general, substitution in the 5,5′-positions, whether by CH_3, halogen, or alkoxy, causes a definite shift toward bluer shades. Halogen groups are not only used to obtain color modifications in the thioindigo series, but the dyes produced are much more stable to light. A multitude of combinations of halogen and methyl substituted thioindigos have been listed in the literature. The classical significance of this tremendous work, carried out principally by German dye chemists of the I.G. Farbenindustrie, has been previously noted (see Chapter II, section VI). No attempt has been made to correlate all of the colors in the patent literature of the many hundreds of isomeric halomethylthioindigos.

The effect of groups such as alkoxy or thioalkyl appears to be to shift the color from red to scarlet. Auxochromic groups, such as hydroxyl or sulfo, appear to deepen the original red color of the dye. Amino groups on the benzenoid rings have a varying effect dependent on the position of substitution; 4,4′-diaminothioindigo dyes cotton in shades intermediate between ultramarine and cornflower blue (222), 5,5′-diaminothioindigo gives greenish-black shades (P-285), 6,6′-diaminothioindigo gives orange shades (P-285) and 7,7′-diaminothioindigo (Table III-1, Thioindigo Gray 2B and Helindon Gray 2B) gives gray shades. Friedländer (208) found that a 6,6′-dimethoxythioindigo gave orange-red shades, the 5,5′-dimethoxy derivative gave bluish-violet shades, while the 4,4′-dimethoxy derivative gave almost the same red shade as thioindigo itself. Introduction of the SO_3H group, Friedländer found, caused a very small change in shade, 5,5′- and 6,6′-thioindigodisulfonic acids differ very slightly from one another.

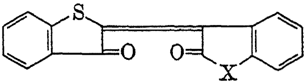
In the asymmetrical thioindigo and thioindirubin series, the replacement of the heteroatom by other atoms or groups causes a series of color changes.



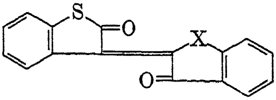
X = NH, red-violet
X = S, red
X = Se, dark red
X = O, yellowish-green
X = CO, red-violet
X = CH_2, red-brown
X = —CH=CH—, violet-red
X = —CH_2—CH_2—, red-violet



X = NH, violet
X = S, violet-black
X = O, yellow-orange
X = CH_2, red-brown

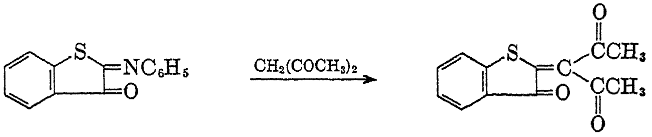


X = NH, scarlet
X = S, red
X = O, light red
X = CO, red-violet
X = CH_2, red-violet



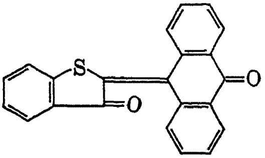
X = NH, scarlet
X = S, red
X = O, orange
X = CH_2, red-brown
X = —CH=CH—, violet

The presence of the benzene ring in asymmetrical thioindigo dyes is not necessary if the chromophoric grouping of the indigo is intact. Herzog and Jolles found that acetylacetone condensed with the anil of 3-hydroxythianaphthene to form a reddish-yellow dye (290) (eq. 49). This is approximately the same color as listed for the 2-thianaphthene-9′-anthroneindolignone (201,437):

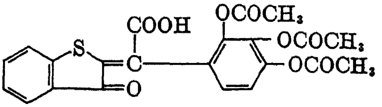


(49)

Reddish-yellow
m.p. 142–143°



and for the 2,3,4-triacetoxy derivative of phenylglyoxylic acid and 3′-hydroxythianaphthene (186).



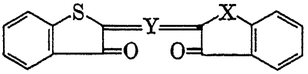
Introduction of selenium (346,347,348,441) for sulfur to produce selenoindigo dyes normally produces reddish-brown shades. The 2-selenonaphthene-2-indoleindigo series gives black-violet shades and appears to be a more deeply colored dye than indigo itself. However, the 2-selenonaphthene-3-indoleindigo series gives red dyes. The 3-selenonaphthene-2-indoleindigo series is bluish-black. The tellurium analogs of this series have not been prepared, since 3-hydroxytelluronaphthene fails to undergo the condensation necessary to form the indigoid group (380).

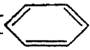
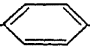
Substitution of a pyridine ring for the benzene ring of thianaphthene (the thienopyridine series) produces a variety of shades. The nitrogen in the 4-position has the strongest auxochromic effect. The colors of three of the four isomeric thienopyridineindigos are as follows:

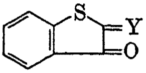
Position of N in benzene ring	Color of symmetrical indigo
4	Dark-violet
5	Intense orange
6	Not synthesized
7	Red

While the nitrogen in the 5-position appears to give a lighter color than thioindigo itself, introduction of methyl groups *ortho* to the nitrogen in the 4- and 6-positions lightens the color still further, producing a light-orange color. For references to the thienopyridines, see Chapter VIII.

The chromophore group in the thioindigo dyes may be extended through a vinylogous system as shown by the following structure:

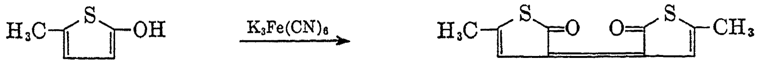


Y is =CH—CH=, =CH—(CH=CH)$_n$—CH=, =CHCH=, or =N—N=, and X has the previous connotation. The colors obtained with the =CH——CH= group are much lighter than those obtained with the alkylpolyene groupings. Somewhat weaker colors are obtained if the chromophoric group is confined to the thianaphthene ring, *e.g.*, as in the formula:



where Y is a =CH—aryl or =N—aryl group (see colors listed in Tables

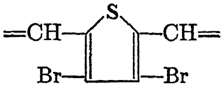
II-14 and II-15, Chapter II, sect. VI). The benzene ring is not essential to the color formation, since 2-hydroxy-5-methylthiophene has also been



Brownish-black with green luster
m.p. 188--190°

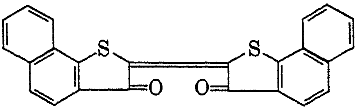
(50)

converted to 5,5′-dimethylbisthiopheneindigo (484) (eq. 50). When Y, in the formula mentioned previously, is:

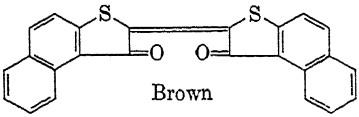


the resultant compound is copper-red, while in the similar condensation product with 5-methyl-2-hydroxythiophene the color is golden-red (484).

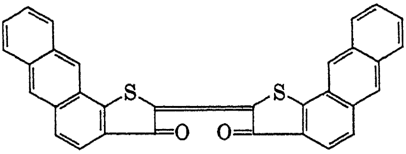
The acenaphthenequinone condensation product of thioindoxyl is scarlet. Introduction of another benzenoid ring in the 5,6-position produces a shift in color from scarlet to brown (351). This is the same relationship previously pointed out for substitution of a benzo group in the benzenoid portion of the thianaphthene ring regardless of position. This latter observation does not hold true when a naphtho group is fused to the benzene ring (P-255). (The benzo analog is shown for comparison.)



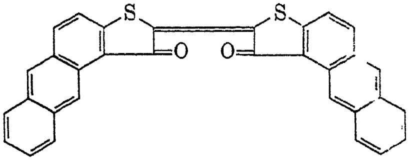
Brown



Brown

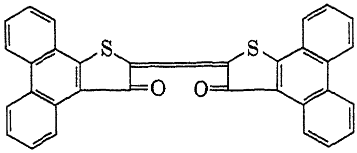


Brownish-yellow

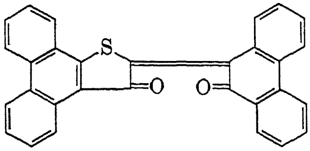


Bordeaux red

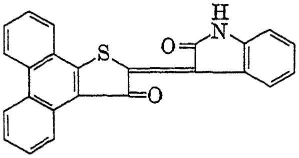
Dutta (167) has shown that two benzene groups fused to the benzene ring of the thianaphthene group give brownish shades in the symmetrical dyes. However, in the asymmetrical series, the colors on cotton changed from brown to red shades.



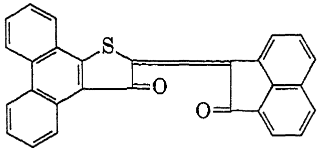
Chocolate



Chocolate-violet



Red



Scarlet-red

For general interest a series of miscellaneous dye compositions and their colors on cotton are compiled in Table III-2. The patent literature has been consulted only in a cursory manner in preparing this table and probably many other comparisons could be made based on that source. The preparation of these complex ring systems is described with full references under the proper categories in subsequent chapters.

IX. Indophenine and Related Dyes

In 1879, Adolph von Baeyer (584) announced the formation of a blue reaction product of "benzene" and isatin in the presence of sulfuric acid. Baeyer had used the purest grade of commercial benzene available at that time and the presence of thiophene in about 1% concentration was not suspected. Unfortunately, the analyses also indicated this compound to be a product of benzene and isatin. Baeyer assigned the formula $C_{20}H_{15}NO$ to this new blue dye, "indophenine." Bromobenzene would not undergo the reaction, but bromoisatin gave a "bromoindophenine," also a blue dye. The yields were extremely low and no attempts were made to commercialize the products. This reaction, however, became a familiar test for "aromatic hydrocarbons" and led directly to the discovery of thiophene by Victor Meyer in 1882. A more detailed discussion of the discovery of thiophene is given in *Thiophene and Its Derivatives* (700), pages 1–4.

With the discovery of thiophene by Victor Meyer, Baeyer's indophenine and bromoindophenine were reanalyzed and the empirical formulas $C_{12}H_7NOS$ and $C_{12}H_6BrNOS$ were assigned (585). Baeyer and Lazarus (587) later prepared these materials from pure thiophene and reported correct analyses.

TABLE III-2. Colors of Miscellaneous Dyes

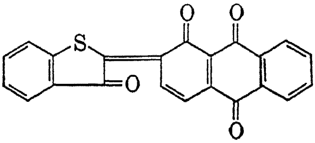
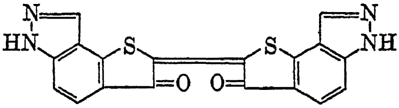
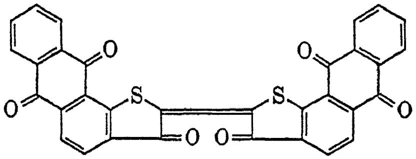
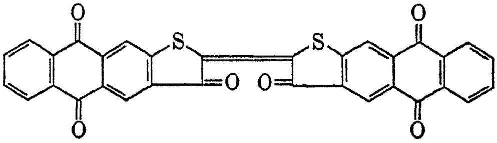
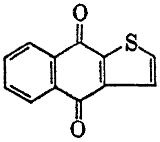
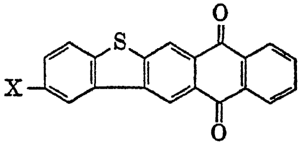
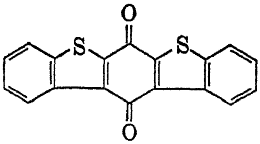
Dye	Color on cotton	Ref.
	Blue	P-32, P-362
	Gray	P-196
	Brown	P-121, P-552
	Helio- trope Green	P-254 P-173
	Yellow	467
 $X = Cl, Br, NO_2$	Yellow	P-794
	Yellow	P-104

Table continued

TABLE III-2 (*continued*)

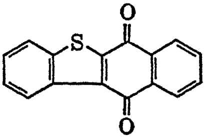
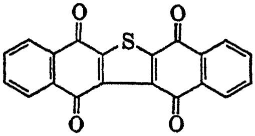
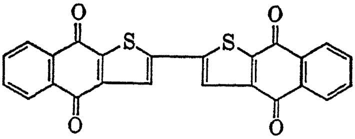
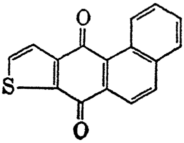
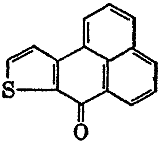
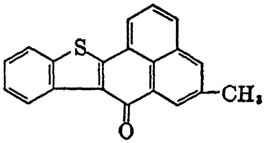
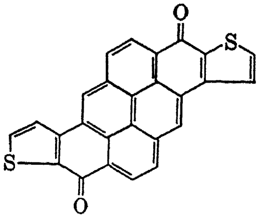
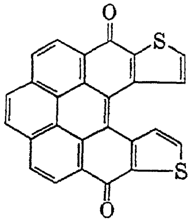
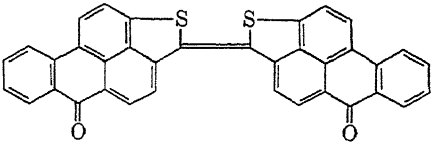
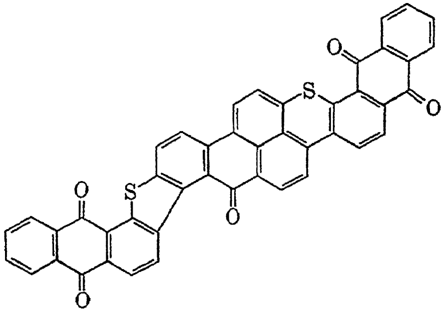
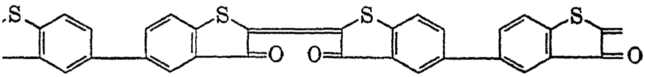
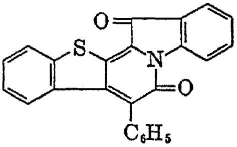
Dye	Color on cotton	Ref.
	Yellow	P-68, P-415
	Dark red	64
	Wine red	486
	Orange	438
	Violet	442
	Blue-gray	P-439
	Red-brown	442

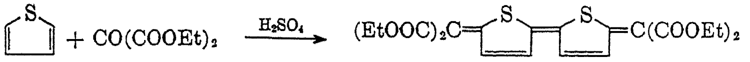
Table continued

LE III-2 (*continued*)

Dye	Color on cotton	Ref.
	Brown	442
	Blue-green	P-192
	Blue-gray	P-601
	Blue	P-341
	Wool, orange-red	**P-379**

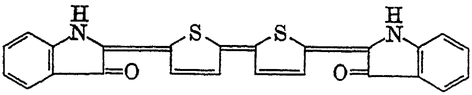
The indophenine test has been used extensively for the detection of thiophene in benzene and is reported to be sensitive to 0.025% of thiophene in benzene (590). The reaction appears to be general for a thiophene nucleus in which the 2,5-positions or the 2,3-positions are unsubstituted (601). In addition, 2-hydroxythiophene (674) gives a blue color; thiophthene gives two blue compounds [$C_8H_4NO \cdot C_6H_3S_2$ and $(C_8H_4NO)_2 \cdot C_6H_2S_2$] and a brown compound [$C_{31}H_{18}O_2N_2S_6$] (600). Presumably, thianaphthene will give the test color since its 4-hydroxy derivative does (49). Conditions for producing the blue test color do not appear to be confined to isatin, since isatinic acid (589), phenanthraquinone (586), phenylglyoxylic acid (586), and benzil (601) give highly colored products. The color in the latter cases is not always blue. Steinkopf and Hanske concluded from these reactions that the thiophene compounds must have the 2,3- or 2,5-positions unsubstituted and the reaction must split out two moles of water from two moles of the thiophene compound and two moles of a —COCO— compound. An oxidizing agent is not necessary. (Considerable discussion concerning the need of an oxidizing agent in this reaction has been published—591,592,594,596.)

The first structure of indophenine and indopheninic compounds to be tentatively accepted was adduced by Schlenk and Blum (597) in 1923 through a series of correlated facts. First, they were able to condense diethyl mesooxalate and thiophene. The resultant product was a deep-violet dye whose empirical formula was given as $C_{22}H_{24}O_8S_2$ (eq. 51).

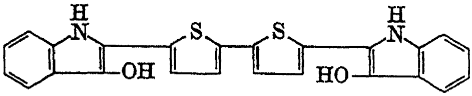


(51)

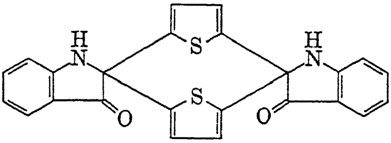
Since Thol (588) had shown that 2,2′-dithienyl underwent the indophenine test, Schlenk and Blum proposed for indophenine the following formula:



They indicated that indophenine could be vatted (*i.e.*, reduced) to the colorless leuco form:

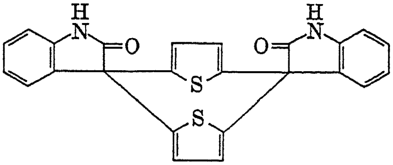


A second formula proposed earlier by Leibermann and Krauss (595):

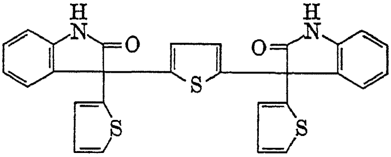


was discarded since it could not form a reversible leuco base on reduction. A year later, Heller (598) published a theoretical discussion of the structure proposed by Schlenk and Blum.

Steinkopf and coworkers (599–602) studied this reaction more thoroughly than others and for a time questioned the structure proposed by Schlenk and Blum to the basis of experiments which indicated that a series of products could be obtained from thiophene, dithienyl, and other thiophene compounds with isatin (599,600). For example, with sulfuric acid, the investigators obtained the standard indophenine with thiophene and isatin in 2:2 molecular ratio. However, in the presence of zinc chloride, a new composition was formed containing two moles of isatin and three of thiophene. The following structures were proposed (599):



(A)



(B)

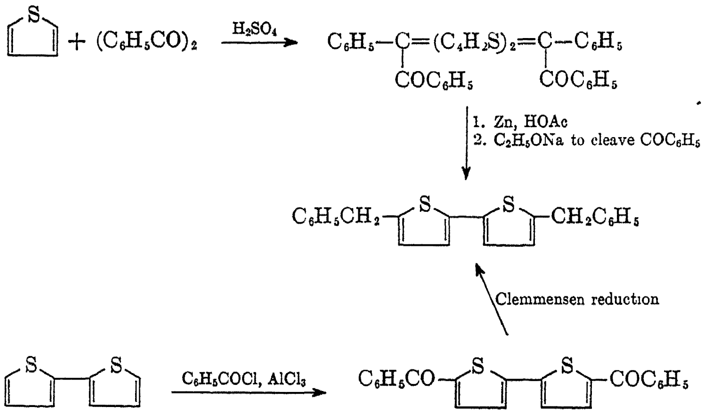
Formula A is equivalent to the Liebermann and Krauss formula with the exception that the 3-oxo group of isatin has reacted rather than the 2-oxo group. This was based on more accurate knowledge of the reactions of isatin than was available to Liebermann and Krauss.

At the same time, Steinkopf and Roch (599) found that dithienyl reacted with isatin to form two compounds of the same molecular ratios as thiophene (*i.e.*, 2:2 and 2:3) and this strengthened their conclusions concerning the structure A.

Subsequent work by Steinkopf and Hanske confirmed the presence of the dithienyl linkage in the condensation products of Schlenk and Blum with thiophene and diethyl mesoxalate and in the condensation product of benzil and thiophene.

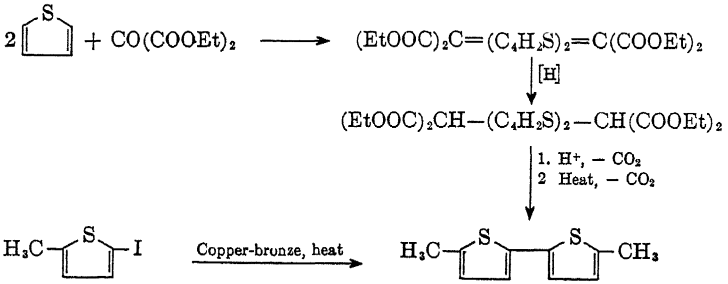
Scheme of Reactions Proving the Presence of the Dithienyl Nucleus

1. From Condensation of Benzil and Thiophene



(52)

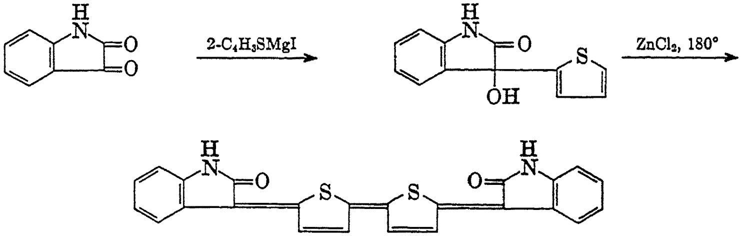
2. From Condensation of Diethyl Mesoxalate and Thiophene



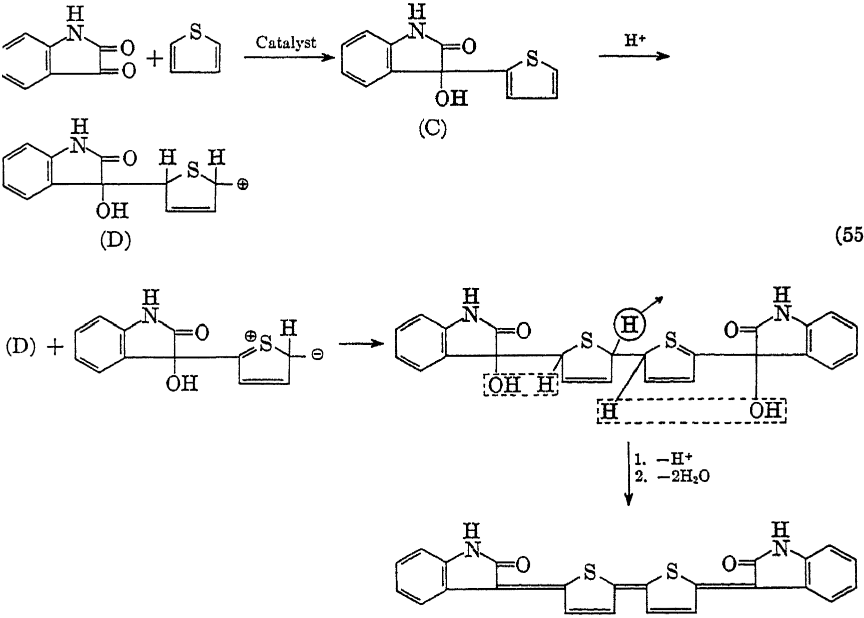
(53)

From a further series of reactions, Steinkopf and Hanske arrived at what is now accepted as the correct formula for indophenine (eq. 54).

On the basis of the work on polymerization of thiophene by acids (603) the probable mechanism for the condensation of isatin and thiophene can be written (eq. 55).

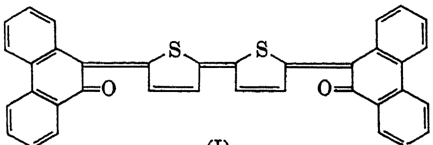


(54)



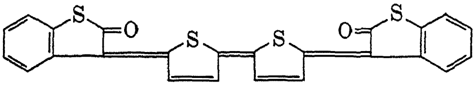
(55)

Although little attention has been given to the reaction of thiophene and phenanthraquinone (586), the resultant green dye, is probably of the same general structure (I):

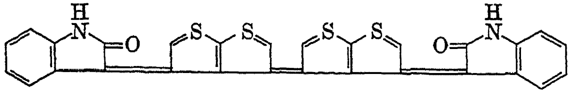


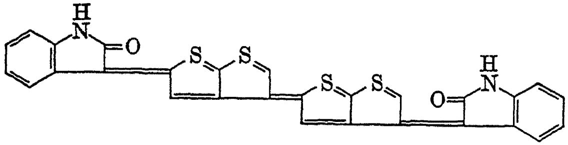
(I)

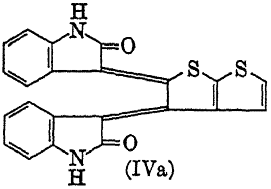
and the blue condensation product of thiophene and 2,3-thianaphthenequinone (46) is probably represented by structure (II):


(II)

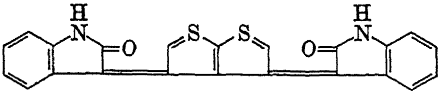
Oster's "carboindophenine" (593) obtained by the condensation of phthalonimide and thiophene probably contains the "dithienyl" central linkage. However, it is difficult to visualize such a structure for the reaction product of thieno[2,3-*b*]thiophene with isatin. Oster (593) described two blue products; one was a 1:1 condensation [$C_8H_4NO \cdot C_6H_2S_2$] and the other had a 2:1 mole ratio [$(C_8H_4NO)_2 \cdot C_6H_2S_2$]. The first probably has a more complex structure than that represented by the simple molecular ratio. Possible structural formulas for these two compounds are represented by III and IV:

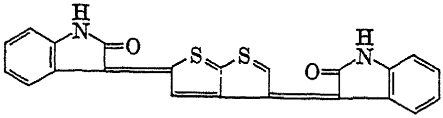

(IIIa, 1:1)


(IIIb, 1:1)


(IVa)

or


(2:1) (IVb)


(IVc)

If one attempts to draw formulas III and IV with the double bonds at the 2,5-positions, not all of the valences of the thiophene nucleus can be satisfied.

Index of References Pertaining to the Thioindigo Dyes Not in Text

Numbers refer to bibliography at end of volume

4
5
8
9
10
42
47
48
66
91
95
113
115
142
147
175
178
182
186
189
195
198
199
200
207
209
210
211
213
215
216
220
221
222
229
243
245
246
251
252
277
283
286
291
292
297
310
313
315
316
322
323
345
349
354
356
365
366
368
370
371
372
373
374
380
383
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393
399
401
402
404
405
406
407
408
414
417
418
419
422
423
428
430
431
432
435
452
453
454
455
456
457
483
491
494
497
498
507
513
515
517
528
529
530
551
567
571
572
618
666
707
708
710
718
720
727
728
732
760

Index of References Pertaining to Naphthothioindigos and Thioindigos Having More Complex Ring Systems Not Included in Preceding Index or Text

15
40
116
172
173
174
185
205
228
230
285
299
308
333
335
355
375
378
434
460
461
462
467
478
486
492
493
495
509
521
550

United States Patents Pertaining to Thioindigos

819,348
831,844
836,309
841,003
848,354
848,355
848,356
850,827
867,305
867,306
867,679
867,714
867,715
868,295
872,085
872,086
872,585
874,649
876,839
877,743
881,157
881,158
881,159
881,624
887,609
888,852
891,690
892,897
893,468
893,499
894,005
894,006
898,738
899,152
899,994
910,839
915,346
916,029
916,030
923,959
941,152
943,678
947,030
949,592
954,273
955,699
959,617
963,813
965,170
968,697
997,260
1,025,138
1,081,898
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1,108,057
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1,202,821
1,243,170
1,243,171
1,247,927
1,261,858
1,434,983
1,444,277
1,448,251
1,461,435
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1,567,158
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1,610,539
1,613,275
1,623,410
1,631,865
1,632,252
1,639,206
1,650,139
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1,655,697
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1,694,413
1,707,918
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1,710,981
1,712,721
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1,728,987
1,730,209
1,730,699
1,733,458
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1,747,107
1,755,667
1,755,972
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1,771,763
1,778,076
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1,784,452
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1,793,648
1,801,713
1,803,008
1,810,758
1,815,990
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1,818,878
1,821,705
1,822,967
1,826,720
1,826,721
1,826,811
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1,850,758

* Reissue 16,939.

United States Patents Pertaining to Thioindigos *(continued)*

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1,857,264
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1,876,930
1,877,316
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1,877,973
1,878,964
1,879,028
1,880,996
1,890,718
1,895,382
1,900,172
1,903,175
1,907,281
1,913,484
1,925,217
1,930,409
1,938,054
1,945,221
1,945,484
1,945,923
1,947,655
1,954,702
1,959,474
1,961,628
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1,972,177
1,976,185
1,979,469
1,983,888
1,989,784
1,990,010
1,990,256
1,990,854
1,995,557
2,000,033
2,000,133
2,003,641
2,004,458
2,005,041
2,007,094
2,021,267
2,022,748
2,024,502
2,027,890
2,029,351
2,029,714
2,032,458
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2,035,325
2,035,361
2,035,362
2,044,790
2,044,796
2,045,475
2,045,476
2,046,267
2,053,821
2,061,186
2,061,200
2,062,443
2,063,147
2,063,161
2,065,928
2,067,926
2,067,927
2,067,928
2,067,929
2,067,930
2,069,215
2,070,739
2,074,150
2,074,380
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2,079,788
2,080,862
2,082,178
2,085,145
2,086,574
2,090,511
2,094,596
2,094,597
2,096,140
2,096,141
2,101,828
2,110,081
2,115,317
2,126,964
2,127,483
2,127,484
2,128,599
2,129,014
2,133,288
2,136,427
2,136,428
2,145,193
2,146,646
2,151,984
2,154,709
2,155,135
2,158,032
2,159,195
2,173,506
2,173,824
2,174,005
2,174,118
2,174,372
2,174,486
2,176,011
2,176,403
2,182,963
2,182,964
2,193,749
2,193,751
2,201,010
2,201,042
2,205,032
2,207,233
2,211,126
2,232,470
2,233,101
2,250,630
2,253,641
2,254,354
2,255,778
2,256,806
2,256,807
2,256,808
2,259,618
2,267,609
2,285,511
2,286,262
2,290,435
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2,315,195
2,318,439
2,327,405
2,334,812
2,354,463
2,356,823

(continued)

United States Patents Pertaining to Thioindigos (*continued*)

2,356,824
2,359,862
2,369,414
2,371,101
2,371,102
2,371,103
2,371,104
2,371,145
2,372,370
2,382,188
2,383,393
2,394,918
2,396,908*
2,397,928
2,402,167
2,403,226
2,405,151
2,406,586
2,415,379
2,420,729
2,428,833
2,428,835
2,432,041
2,450,767
2,451,270
2,453,225
2,472,356
2,475,821
2,487,197
2,493,072
2,528,614

German Patents Pertaining to Thioindigos

177,345
177,346
177,347
182,260
182,261
184,496
184,956
187,586
188,702
190,291
190,292
190,293
190,477
190,674
191,097
191,098
191,112
192,075
193,150
194,040
194,237
194,254
196,016
196,349
196,501
196,658
197,057
197,150
197,162
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198,509
198,644
198,645
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198,712
198,713
198,864
199,349
199,492
199,551
199,619
200,200
200,202
200,351
200,428
200,593
200,927
201,231
201,232
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202,351
202,696
202,707
202,708
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203,029
204,602
204,763
205,002
205,324
205,377
206,537
206,538
206,567
206,568
207,574
208,343
208,499
209,122
209,576
210,644
210,682
210,813
210,905
211,696
212,782
212,791
212,870
212,942
213,458
213,465
213,474
213,504
213,505
213,714
214,715
214,781
215,785

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* Re-issue 23,004.

German Patents Pertaining to Thioindigos *(continued)*

216,224
217,556
218,992
219,268
219,830
221,216
221,261
221,465
221,529
221,530
224,158
224,205
224,567
225,132
225,242
226,244
228,914
229,067
229,267
229,369
230,308
230,641
231,927
232,069
232,277
232,714
232,995
233,473
233,601
233,741
234,058
234,375
235,625
235,811
236,536
237,395
237,680
239,089
239,090
239,091
239,092
239,093
239,094
239,673
239,674
239,916
240,118
240,805
241,326
241,327
241,343
241,623
241,839
241,910
242,220
242,461
242,997
242,998
243,087
243,536
244,615
244,616
245,544
245,630
245,631
245,632
245,633
246,265
246,581
248,083
248,263
248,264
250,157
250,464
252,771
253,762
254,364
254,468
258,099
259,145
261,930
263,470
265,536
270,334
273,536
273,537
274,299
277,197
277,358
280,649
282,890
283,356
286,151
291,759
292,171
293,113
321,119
325,562
326,573
342,896
343,596
360,425
362,551
367,493
371,258
374,503
380,712
386,889
400,630
402,994
403,053
403,274
410,310
411,652
413,941
414,084
414,260
419,867
424,981
427,997
428,241
430,548
433,290
435,787
436,176
439,290
440,827
441,101
445,218
445,443
445,566
450,799
450,852
451,411
451,549
453,087
453,718
455,280
455,882
456,863
456,864
461,490
461,503
463,001

(continued)

German Patents Pertaining to Thioindigos *(continued)*

464,087
465,971
466,535
466,938
469,178
469,248
469,249
469,326
469,342
470,759
472,341
474,036
479,487
479,678
481,598
481,599
483,154
483,232
483,233
486,174
489,087
489,725
490,599
491,876
493,410
494,597
494,948
494,949
495,732
496,339
504,076
504,409
504,628
512,483
513,230
513,357
513,358
517,444
518,951
519,265
519,747
519,984
521,051
521,476
524,828
525,302
525,668
530,907
531,473
532,256
533,151
533,796
534,642
535,143
535,249
538,313
538,315
539,468
540,470
540,619
540,861
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541,073
542,176
542,177
543,462
545,114
546,005
546,006
547,925
548,820
552,927
556,486
557,127
557,233
557,826
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564,115
564,770
564,823
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570,766
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571,241
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574,940
575,788
578,322
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583,649
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596,887
598,678
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601,721
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601,860
602,095
604,014
604,468
606,563
616,074
617,726
617,727
622,761
622,985
623,554
623,589
623,713
624,638
626,626
626,627
626,811
626,812
626,862
627,389
627,390
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627,468
627,903
628,303
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630,207
630,221
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631,655
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633,103
633,354

German Patents Pertaining to Thioindigos *(continued)*

633,522
633,836
634,041
636,208
636,269
637,210
637,274
638,450
639,185
659,653
661,136
661,811
662,936
663,216
663,314
668,386
670,472
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678,131
679,767
691,176
692,895
694,602
696,268
699,029
700,758
717,076
724,848
734,399
735,093
736,882
739,049
743,221
743,676
745,417

British Patents Pertaining to Thioindigos

22,316/05
4,687/06
14,191/06
14,507/06
16,100/06
17,162/06
17,559/06
22,736/06
26,190/06
1,472/07
1,593/07
1,594/07
2,592/07
2,769/07
8,162/07
11,609/07
15,607/07
16,584/07
19,158/07
26,053/07
344/08
2,769/08
4,541/08
5,589/08
8,381/08
8,531/08
10,755/08
16,017/08
20,003/08
20,200/08
5,558/09
14,314/09
16,017/09
16,996/09
17,265/09
18,117/09
21,578/09
21,579/09
21,580/09
23,873/09
28,170/09
5,670/10
6,351/10
12,321/10
19,340/10
24,569/10
2,732/11
13,550/11
22,067/11
28,656/12
29,583/12
10,583/13
22,287/13
18,292/14
186,057
189,782
198,415
202,630
202,632
202,734
209,092
210,413
211,120
214,864
222,094
222,120
225,544
226,373
231,567
231,889
232,230
232,252
233,831
234,928
235,252
235,877
236,332
237,295
247,787
249,489
250,251
251,293
251,321
251,996
251,997
254,340
254,743
258,626
259,999
260,303
260,940
262,457
266,382
267,177
267,952
271,906
274,094
274,156
274,527

(continued)

British Patents Pertaining to Thioindigos (*continued*)

275,292
276,023
279,489
281,336
282,805
283,118
284,288
285,389
286,359
288,215
288,554
291,361
291,768
292,622
292,904
295,239
295,593
295,716
297,376
298,088
299,743
299,899
300,114
302,175
304,794
309,379
309,970
310,437
310,478
310,803
311,047
312,347
313,407
313,493
314,350
318,178
318,595
319,021
330,579
334,878
334,907
334,920
340,085
341,224
342,407
343,527
344,964
345,130
345,349
345,743
349,955
350,862
350,963
354,716
355,661
355,662
356,577
357,592
357,593
359,426
360,533
360,583
360,907
360,958
361,165
361,350
361,406
364,052
368,505
368,726
371,459
371,826
372,640
373,601
377,024
378,553
380,020
380,860
380,902
383,543
383,662
389,350
389,915
390,081
395,183
396,636
398,053
398,161
402,265
405,092
406,914
407,578
407,702
413,344
414,426
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422,595
422,690
425,841
426,073
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427,248
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520,391
520,415
522,127
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541,097
547,411
547,629
548,806
556,486
585,106
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588,106
600,944
607,608
616,440
619,357
624,491
631,907
633,478
633,487
633,492

French Patents Pertaining to Thioindigos

336,875
348,360
359,398
359,400
362,876
366,613
366,875
367,431
367,709
367,739
367,772
368,317
368,775
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373,513
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378,406
383,515
383,927
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417,947
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432,791
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718,113
720,382
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721,087
721,137
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758,261
764,012

(continued)

French Patents Pertaining to Thioindigos (*continued*)

765,377
765,744
766,452
769,171
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45,824/774,286
776,153
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823,196
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847,143
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914,417
926,334
929,669
966,774

CHAPTER IV

Dibenzothiophene and Its Derivatives

I. Introduction

The reactions of dibenzothiophene differ markedly from those of thianaphthene, and the isomeric naphthothiophenes. Dibenzothiophene is singularly different from these other materials in that it contains a ring system that cannot be substituted at a carbon atom in the thiophene nucleus. For that reason, its reactions are more typical of an aromatic compound than of a condensed thiophene.

Dibenzothiophene undergoes most of the substitution reactions commonly associated with aromatic compounds: bromination, nitration, acylation, and sulfonation. It is also easily metalated and this reaction has been extremely useful for the preparation of a large number of derivatives.

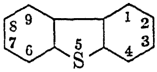
The sulfur atom exerts a considerable directive influence on incoming electrophilic groups, mono- and dinuclear substitution occurring predominantly at the 2- and 2,8-positions, respectively. Metalation occurs at the 4-position. The few orientation studies of dibenzothiophene substituted by a ring-activating group such as —$NHCOCH_3$ or —OCH_3 indicate that, irrespective of the position of the substituent, further substitution occurs in the ring containing the activating group. The positions at which substitution occurs in the alkyldibenzothiophene series have not been reported. Orientation effects are discussed in greater detail in Chapter I.

The sulfur atom can completely alter the course of some reactions. For example, when dibenzothiophene is chlorinated at low temperatures, addition occurs at the sulfur atom. The sulfur atom is also easily oxidized to a sulfoxide or sulfone. These groups exert a directive influence at the 3- and 3,6-positions, making these isomers readily available. The sulfones have also played an important role in establishing the structures of dibenzothiophene derivatives, since they can be cleaved by caustic to yield substituted biphenyls.

II. Dibenzothiophene

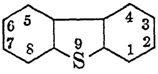
A. Nomenclature

Preferred Numbering



Ring Index No. 1743
$C_{12}H_8S$

Other Numbering



Preferred Name
Dibenzothiophene

Other Names
Biphenylene Sulfide
Diphenylene Sulfide

The numbering system that is currently widely accepted for dibenzothiophene (S = 5) was adopted by *Chemical Abstracts* in 1937 (Volume 31) Prior to this time, the older numbering system (S = 9) was used.

The name *dibenzothiophene* has always been used by *Chemical Abstracts.* The other names, *biphenylene sulfide* and *diphenylene sulfide,* have appeared extensively in the past German literature, but, at present, *dibenzothiophene* is the accepted name.

B. Occurrence in Nature

There are very few references in the literature regarding the natural occurrence of dibenzothiophene. Kramer and Weissgerber (332) noted, during their investigations of coal tar fractions, that commercial fluorene contained small amounts of sulfur. They stated that these materials were probably dibenzothiophenes, and predicted that larger amounts of these dibenzothiophenes should be present in the liquid portions of coal tar fractions. By treating crude phenanthrene with acetic acid and hydrogen peroxide, Kruber (336) succeeded in separating out the dibenzothiophene in the form of its sulfone, m.p. 229–230°. Weissgerber (523) also mentions the isolation of pure dibenzothiophene from the crude phenanthrene portion of tar oil.

Dibenzothiophene has been found in the bitumen extracted by aniline from coal of the Lenin mine (276). The authors suggested that this material existed within the coal itself and was probably formed during the carbonization period.

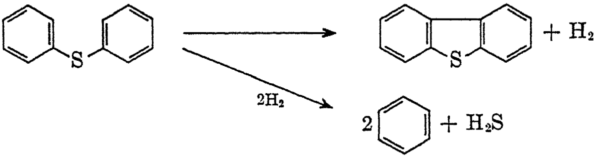
Recently, dibenzothiophene-type compounds have been reported to be present in a Middle East gas oil (boiling range (260–350°C.) (626). Dibenzothiophene is not selectively soluble in anhydrous liquid hydrofluoric acid and it can be separated by this means from the other thiophene compounds that are present.

C. Preparation

1. Historical

Dibenzothiophene was first prepared by Stenhouse (489) in 1870 by placing diphenyl sulfide in an iron tube filled with nails and heating the tube until it glowed. A solid material melting at 94° could be separated from the reaction mixture. Analysis of this material indicated an empirical formula of $C_{12}H_{10}S$, which is isomeric with diphenyl sulfide, and Stenhouse accordingly referred to it as *paraphenyl sulfide*.

Four years later, Graebe (248,247) published a paper stating that on the basis of Kekulé's recently proposed structures for benzene, diphenyl sulfide could not exist in more than one modification, and therefore Stenhouse's *paraphenylsulfide* could not be a structural isomer of diphenyl sulfide. Graebe repeated Stenhouse's work and showed that hydrogen, benzene, and hydrogen sulfide were also formed in the reaction. In addition, the solid material analyzed for $C_{12}H_8S$ rather than $C_{12}H_{10}S$ as reported by Stenhouse. Graebe correctly concluded that dehydrocyclization must have taken place and that the solid material was diphenylene sulfide (dibenzothiophene). He suggested equations 1 to account for the products.

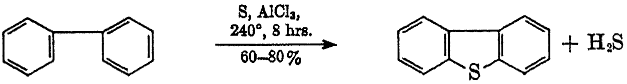


(1)

The elucidation of the correct structure of dibenzothiophene by Graebe was a remarkable contribution, considering that the parent compound, thiophene, was not discovered for another ten years. Graebe, at this time, was also studying the structures of carbazole and phenanthrene, and comparisons of these three materials undoubtedly had much to do with his correct deductions.

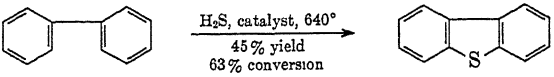
2. Cyclization of Biphenyls

The best reported method for the preparation of dibenzothiophene consists of reacting biphenyl with sulfur in the presence of aluminum chloride (P-459,P-648,392,231). Distillation of the dibenzothiophene affords a very pure product (eq. 2).



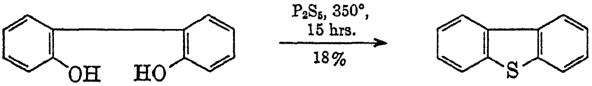
(2)

Dibenzothiophene has also been made by a somewhat similar method from biphenyl and hydrogen sulfide in the presence of a reforming catalyst (eq. 3). The catalyst was composed of 85% Al_2O_3, 10% Cr_2O_3 and 5% SiO_2.



(3)

Approximately equal yields (18%) of dibenzothiophene have been obtained from the fusion of either phosphorus pentasulfide or sulfur with 2,2′-dihydroxybiphenyl (P-385,135). The 2,2′-dihydroxybiphenyl was made by fusion of dibenzofuran with alkali (eq. 4).

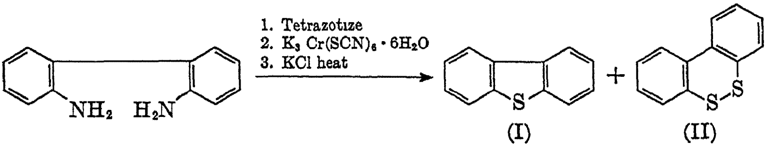


(4)

This process is similar to the method used by Paal (647) for the conversion of acetonylacetone to 2,5-dimethylthiophene, and it certainly supports the view that the latter reaction proceeds through the enol form.

2-Hydroxybiphenyl has also been cyclized (25% yield) to dibenzothiophene by phosphorus pentasulfide (135).

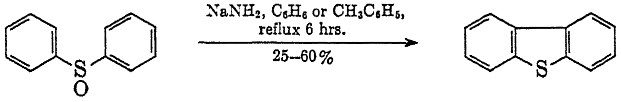
2,2′-Diaminobiphenyl can be converted to dibenzothiophene by the procedure of eq. 5 (450). Although specific yields were not reported, it was indicated that the yields were high. A small amount of dibenzo[*ce*]-*o*-dithiin (II) (2,2′-diphenylene disulfide) is also formed, but the crude mixture can be converted to pure dibenzothiophene by distilling from copper-bronze. Heating II at 250° for 2 hours with copper also yields I (30).



(5)

3. Cyclization of Sulfur Compounds

A number of investigators have prepared dibenzothiophene from diphenyl sulfoxide (III) (eq. 6) and sodamide (443,125,392,136,134). Ani-

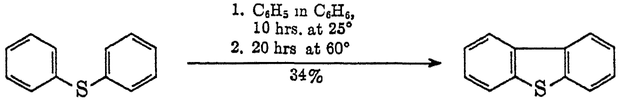


(III) (I) (6)

line, diphenyl disulfide, and benzenesulfinic acid have been isolated as byproducts of this reaction (125). Phosphorus pentoxide also converts III to I, but in yields much lower than those obtained with alkali amides (P-398).

A 50% conversion of III to I is obtained with phenylsodium as a condensing agent (223). Replacement of phenylsodium by benzylsodium affords an extremely poor yield of I. As expected, no dibenzothiophene is formed when diphenyl sulfoxide is replaced with phenyl benzyl sulfoxide.

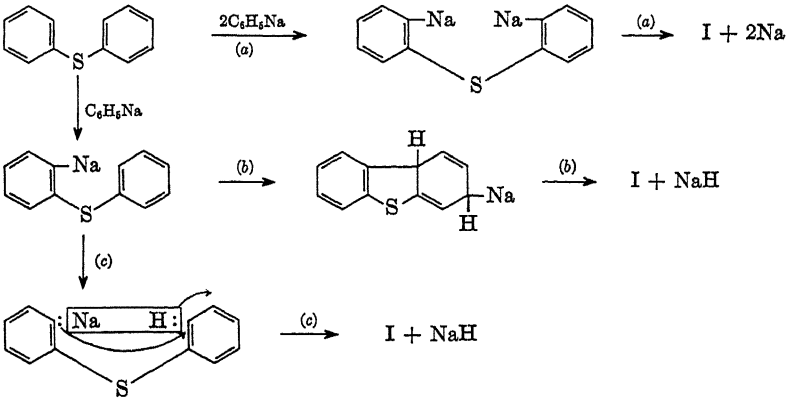
Diphenylsulfide has also been cyclized to dibenzothiophene by means of phenylsodium (357) (eq. 7). In addition, thiophenol and resinous ma-



(I) (7)

terials are formed. Only a 10% yield of I is obtained when the phenylsodium is replaced with phenyllithium.

Several interesting mechanisms have been proposed to account for the formation of dibenzothiophene (I) from diphenyl sulfide (eq. 8). The



(8)

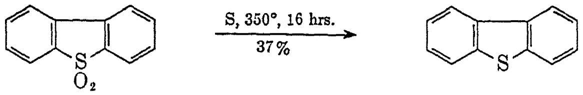
first mechanism (*a*) involves dimetalation of the diphenyl sulfide followed by the expulsion of 2 sodium atoms. In the second mechanism (*b*), monometalation occurs initially. This is then followed by an internal rearrangement involving a 1,4-addition in which the ring is closed and sodium is added to the 4-position, forming a *p*-quinoid structure. Elimination of sodium hydride from the material yields I. In the last mechanism (*c*), monometalation is also postulated for the first step. The ionization of the carbon-sodium bond allows the relatively free electrons to form a carbon-carbon bond with the expulsion of a hydride ion. The removal of the hydride ion is also facilitated by the sodium atom which reacts with it to form sodium hydride. This mechanism would not preclude initial removal of a hydride ion by sodium followed by ring closure.

Dibenzothiophene has been prepared in 40% yield from 2-aminodiphenylsulfide (139). Thiophenol and litharge are reported to yield dibenzothiophene in 6% yield (134). Thianthrene, diphenyl sulfide, and diphenyl disulfide have also been isolated from this reaction mixture.

4. Reduction of Oxides and Dioxides

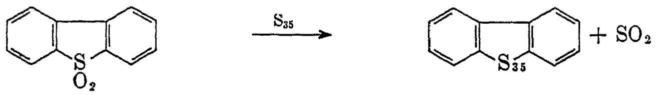
The reduction of dibenzothiophene 5-oxide to dibenzothiophene can be accomplished in high yields (85%) with stannous chloride and concentrated hydrochloric acid (69). The oxide is also reduced by ethylmagnesium bromide (117) and butyllithium (735), but no reaction occurs with phenylmagnesium bromide (117).

The 5-dioxide is considerably more stable toward reduction than the oxide. However, it has been converted to the sulfide in fair yields by heating with molten sulfur (136,231) (eq. 9).



(9)

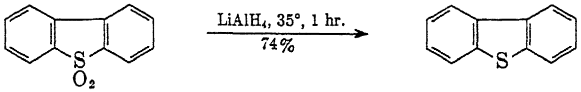
Recent work carried out with radioactive sulfur has thrown some light on the mechanism of this reaction (661). There are two possible routes that this reaction can follow: (*1*) removal of the oxygen atoms by reduction to form sulfur dioxide; and (*2*) replacement of the sulfone group by sulfur. When dibenzothiophene 5-dioxide was reacted with radioactive sulfur, a radioactive dibenzothiophene was obtained. Less than 4% of the radioactive sulfur could be found in the sulfur dioxide and in the small amounts of hydrogen sulfide liberated. This indicates that the sulfone group is replaced rather than reduced by sulfur (eq. 10). Since



(10)

dibenzothiophene 5-oxide is converted to dibenzothiophene much more readily than the dioxide, it would be interesting to effect this reaction with radioactive sulfur and determine whether the replacement or reduction reaction predominates in this case.

Actual reduction of the sulfone group has been accomplished recently with lithium aluminum hydride (677) (eq. 11). This rather easy reduction

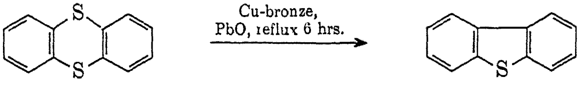


(11)

of the sulfone group should make a number of the 3-substituted and 3,7-disubstituted dibenzothiophenes much more accessible.

5. *Miscellaneous Methods*

The refluxing of thianthrene over copper bronze gives a good yield of dibenzothiophene (137) (eq. 12). The conversion of 2,2′-diphenylene



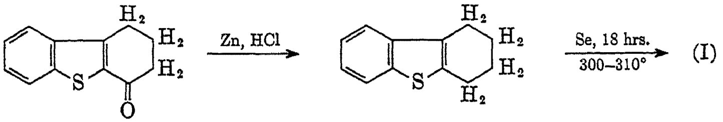
(I)

(12)

disulfide to I has been mentioned previously (30,450).

The fusion of dibenzotellurophene with sulfur has also been reported to yield I.

Dibenzothiophene has been made from 4-oxo-1,2,3,4-tetrahydrodibenzothiophene by the following series of reactions (77) (eq. 13). The



(13)

dehydrogenation with selenium is essentially quantitative.

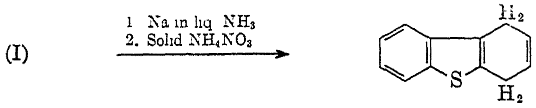
A similar synthesis involving the dehydrogenation of 1,2,3,4-tetrahydrodibenzothiophene has been reported recently (768). The tetrahydrodibenzothiophene was made in 74% yield by treating 2-(phenylthia)-cyclohexanone with phosphorus pentoxide at 170–180° *in vacuo*. 1,2,3,4-Tetrahydrodibenzothiophene is reported to boil at 141° (10 mm.) (768) and at 212–215° (3 mm.) (77) and to form a picrate, m.p. 108–109° (768).

Note added in proof: Cagniant and Cagniant (778) have reported a new synthesis of 1,2,3,4-tetrahydrodibenzothiophene (b.p. 155° (0.5 mm.)) and 1,2,3,4,6,7,8,9-octahydrodibenzothiophene and several of their derivatives.

D. Reduction Reactions of Dibenzothiophene

Only hydrogenation reactions and reactions involving reductive cleavages are discussed in this section. Reactions involving the formation of new derivatives (other than hydro) are discussed in subsequent sections dealing with these derivatives.

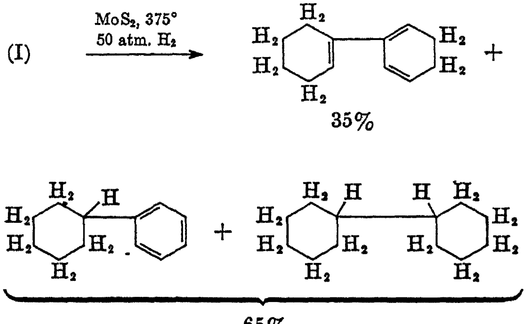
1,4-Dihydrodibenzothiophene has been made by the metalation of dibenzothiophene followed by careful ammonolysis with ammonium nitrate (231) (eq. 14). The dihydro derivative adds theoretical quantities of bromine. Attempts to recrystallize this material were unsuccessful, yielding only dibenzothiophene. 1,4-Dihydrodibenzothiophene can be dehydrogenated smoothly with phenyllithium; dibenzothiophene, benzene, and lithium hydride are the resultant products. Phenylisopropyl potassium may also be used in this dehydrogenation.



(14)

b.p. 160–165° (6 mm.)
m.p. 76°
Picrate, m.p. 105°

Hydrogenation of dibenzothiophene over cobalt or molybdenum sulfide leads to almost complete removal of the sulfur and to partial hydrogenation of the biphenyl derivatives that are produced (626) (eq. 15). The pro-



(15)

cedure used to determine the structure of the hydrogenated biphenyls was not mentioned, although it is presumed that spectrographic methods were used.

Almost quantitative yields of biphenyl can be obtained from dibenzothiophene by dissolving it in alcohol and refluxing the solution with large amounts of Raney nickel (53). This reaction should be of invaluable aid in the determination of the structures of alkyldibenzothiophenes and any other derivatives in which the grouping is not cleaved by the nickel.

E. Properties

1. Physical Properties

Dibenzothiophene is best purified by distillation followed by recrystallization from alcohol. Using this procedure, beautiful colorless needles can be obtained. The reported physical properties of dibenzothiophene are listed in Table IV-1.

TABLE IV-1. Physical Properties of Dibenzothiophene

Property	Reference
B.p. 152–154° (3 mm.)	231
166° (10 mm.)	P-676
182° (10 mm.)	135
M.p., 99–100°	103,231,45,138
M.p. of picrate, 125°	231
123–124°	P-676,768
Dipole moment ($\mu \times 10^{18}$), 0 83	103, 706
0	45
Polarization ($P\alpha$), 49.6	103

A number of spectrographic measurements have been made on dibenzothiophene. Werner (526) has measured the ultraviolet absorption of dibenzothiophene and has found that it shows a strong absorption at 230 mμ and fairly strong absorption at 290 and 325 mμ. Recent ultraviolet absorption spectra have also indicated that dibenzothiophene is a planar molecule (639). Raman spectra studies show a definite displacement of the benzene lines (149). Other absorption and fluorescence spectra have also been reported (350).

Two dipole moments have been reported for dibenzothiophene, 0 (45) and 0.83*D* (183). In view of the large negative charge that must repose at the sulfur atom, attested by its facile oxidation to sulfoxides and sulfones, it is inconceivable that the molecule could have a zero dipole moment.

In fact, Charles and Freiser have correlated sulfone formation with known dipole moments and have found that the larger the dipole moment the greater the ease of formation of the sulfone. On this basis, dibenzothiophene should have a larger dipole moment than the 0.53*D* possessed by thiophene.

Melting point curves of dibenzothiophene admixed with dibenzofuran and dibenzoselenophene have been determined and are shown in Figures 1-3 (138). The melting point curve of dibenzothiophene and dibenzofuran is very unusual, showing a maximum depression of 1.8°, corresponding to 26 mole per cent of the dibenzothiophene. There is no depression in melting point in the dibenzothiophene-dibenzoselenophene curve, all melting points being intermediate between those of the pure compounds. The dibenzoselenophene-dibenzofuran curve was also determined and these compounds form a eutectic corresponding to 35 mole per cent of dibenzofuran.

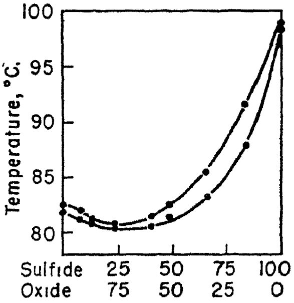


Figure 1

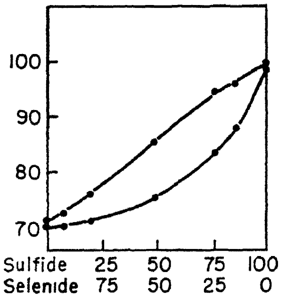


Figure 2

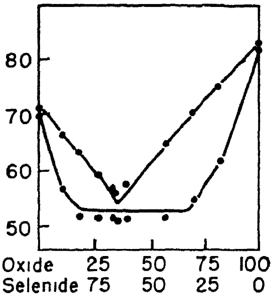


Figure 3

2. Toxicological Properties

Dibenzothiophene has been shown to be very toxic to *Culicine* mosquito larvae. Fink and Smith (187) have found that dibenzothiophene in concentrations of 3.3 p.p.m. killed 50% of these mosquito larvae in 16 hours. Toxicity tests on screw worms, *Culex* larvae (75), produced 100% mortality in concentrations less than 10 p.p.m. Dibenzothiophene was also found to be toxic to the young larvae of *Cochliomyia americana* (463). Thianthrene showed no toxicity to these larvae. Promising results have been obtained in laboratory tests with dibenzothiophene as an insecticide against the pea aphid (*Macrosiphum pisi* Kltb.) (150). It is not effective in chigger control (638). The use of dibenzothiophene with known mothproofing agents is claimed to improve their effectiveness (P-683).

The continued addition of dibenzothiophene to the diets of albino rats resulted in lessened growth with concentrations as low as 0.05% (508). Food consumption varied inversely with the concentration of dibenzothiophene and retardation in growth was attributed primarily to the decrease in food intake. The spleens of the animals decreased in weight as the dose of dibenzothiophene was increased. However, the histology of the organ remained normal and there was no evidence of blood injury.

Dibenzothiophene has also been tested for possible analgesic effect (73). It is relatively inert when administered orally to cats. The same is also true of dibenzofuran, carbazole, and phenanthrene.

3. Miscellaneous Properties

The action of hydrofluoric acid on dibenzothiophene is surprising (539, 626). Although hydrofluoric acid shows a great specificity for thiophene compounds, it has practically no selective solvent power for dibenzothiophene. Use has been made of this property in separating dibenzothiophene-type compounds from other sulfur compounds present in fuel oil.

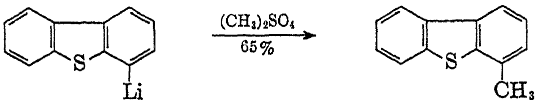
Dibenzothiophene has little or no antioxidant properties (144). A 3% blend of dibenzothiophene in desulfurized oil stock was found to absorb oxygen at 171°C. as fast as the base stock. In contrast, 2-cetylthiophene had considerable effect in slowing down the oxidation.

Dibenzothiophene is reported to give a brown color with ceric nitrate-alcohol reagent (652).

III. Alkyl and Aryl Derivatives of Dibenzothiophene

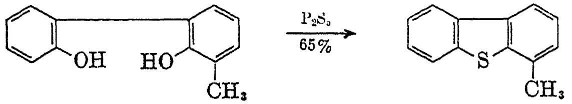
The literature regarding the preparation of alkyldibenzothiophenes is extremely limited. The only reported alkylation of dibenzothiophene in the presence of Friedel-Crafts catalysts is cited in a recent patent (P-690). However, only mixtures of materials were obtained and no attempt was made to isolate pure compounds. It is only recently that the syntheses of alkyldibenzothiophenes having a side chain greater than methyl have been reported (635). Very little is known of the chemistry of alkyldibenzothiophenes. A study of their chemical behavior and physical properties would certainly augment our knowledge of the chemistry of heterocyclic compounds.

4-Methyldibenzothiophene is the only monomethyl derivative that has been synthesized. It was first made by reacting 4-dibenzothienyllithium with dimethyl sulfate (231) (eq. 16).



(16)

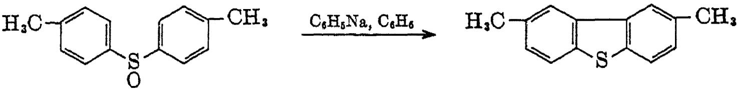
When 4-dibenzothienyllithium is treated with sodamide, rearrangement to the 3-position takes place (see section on aminodibenzothiophenes). In order to make certain that rearrangement did not take place with dimethyl sulfate, 4-methyldibenzothiophene was synthesized from 3-methyl-2,2′-dihydroxybiphenyl and phosphorus pentasulfide (eq. 17).



(17)

Both products were identical showing that no rearrangement took place in the first reaction.

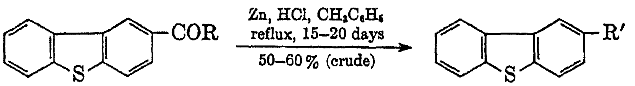
A dimethyldibenzothiophene has been made by heating *p,p′*-ditolyl sulfoxide with phenylsodium (223) (eq. 18). The authors reported the



(18)

material to be 1,9-dimethyldibenzothiophene. No reasons were given for this choice which would involve the shifting of both methyl groups. Since there is no apparent reason for this rearrangement, it seems more likely that, if a dibenzothiophene was formed, it was probably the 2,8-derivative which is shown above. By allowing *p,p′*-ditolyl sulfoxide to react with sodium in benzene solution for one year the same dimethyldibenzothiophene was formed (224). This was established by oxidation to sulfones which when compared with each other produced no depression in melting point.

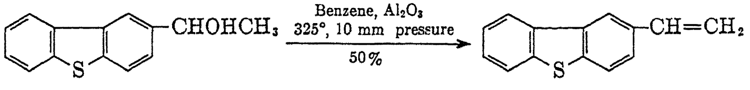
Recently several 2-alkyl derivatives of dibenzothiophene have been prepared by the Clemmensen reduction of the acyl derivatives (613) (eq. 19). In view of the extremely long reaction times, it appears that the Wolff-Kishner reduction might be used more expediently.



$R' = n\text{-}C_7H_{15}$, b.p. 258° at 18mm. (19)
$R' = n\text{-}C_8H_{17}$, b.p. 280–285° at 20mm.
$R' = n\text{-}C_{10}H_{21}$, b.p. 289–290° at 16mm.
$R' = n\text{-}C_{14}H_{29}$, b.p. 305–310° at 12mm.; m.p. 52–53°.

Attempts to acylate 2-*n*-octyl- and 2-*n*-decyldibenzothiophene with propionyl chloride in the presence of aluminum chloride were unsuccessful. This is rather puzzling, since dibenzothiophene undergoes both mono- and diacylation and one would certainly not expect the alkyl group to have a deactivating effect on the unsubstituted ring. Under the same conditions the corresponding dibenzofuran derivatives yield substantial amounts of ketone.

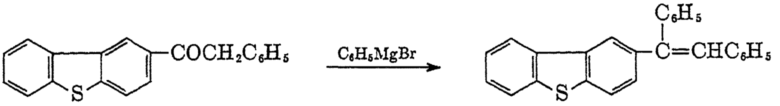
2-Vinyldibenzothiophene has been synthesized by the dehydration of 2-(1′-hydroxyethyl)dibenzothiophene over alumina (188) (eq. 20). The dehydration can also be carried out by heating the alcohol and *p*-tert-butylcatechol until molten and then adding copper sulfate to the molten mass (188,P-668). The *p-tert*-catechol acts as a polymerization inhibitor. 2-Vinyldibenzothiophene has been polymerized at 125° to give a hard brittle mass. It has also been copolymerized with styrene, *N*-vinylcarbazole, *N*-vinylphthalimide, acrylonitrile, and acenaphthylene to give white powders having softening points from 174 to 200°.



(20)

m p. 45–45.5°

1-(2′-Dibenzothienyl)-1,2-diphenylethylene has been made by reacting phenylmagnesium bromide with 2-phenylacetyldibenzothiophene (83) (eq. 21).



(21)

b.p. 320° (17 mm.)
m p. 150°

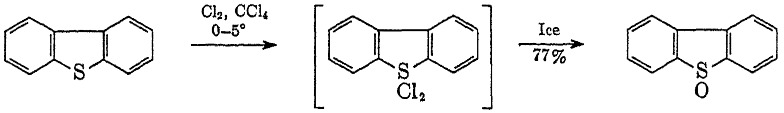
There have been no aryldibenzothiophenes of known structures reported in the literature. Graebe, during the course of his study of the structure of dibenzothiophene, isolated from the reaction mixture a material, m.p. 97°, which analyzed empirically as phenyldibenzothiophene (247). However, no further work on the structure of this material has been reported.

IV. Sulfoxides and Sulfones

The sulfoxides and sulfones are extremely important derivatives of dibenzothiophenes. The sulfones, especially, have been prepared for purposes of identification and proof of structure of various dibenzothiophene derivatives. Monosubstitution of the sulfoxides and sulfones occurs at the 3-position (dibenzothiophene is substituted at the 2-position). This has made it possible to prepare a new series of dibenzothiophene derivatives, since the sulfoxides and sulfones can be reduced to the thiophene ring. Only the oxides of dibenzothiophene and their hydro and alkyl derivatives are discussed in this section. The substituted sulfoxides and sulfones are discussed in subsequent sections.

Dibenzothiophene 5-oxide was first isolated in 40% yield as a by-product from the reaction of dibenzothiophene and nitric acid (117). The amount of sulfoxide can be increased by substituting sulfuric acid for acetic acid in the nitrating mixture. The formation of the oxide as a by-product of the nitration reaction has also been reported by other investigators (119,392).

An excellent method for the preparation of the oxide consists of reacting dibenzothiophene with chlorine to form the dichloride which can then be hydrolyzed (69) (eq. 22). The intermediate dichloride was not isolated.



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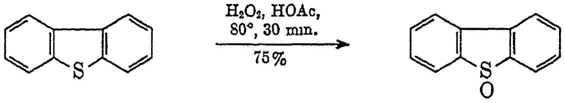
Dibenzothiophene 5-oxide has also been made by the oxidation of dibenzothiophene with limited amounts of hydrogen peroxide (392) (eq. 23).



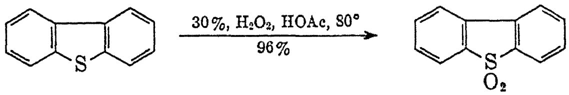
(23)

Although the yield of oxide was high, the reported melting point of 175° is low. This indicates the presence of impurities which are probably unreacted dibenzothiophene and dibenzothiophene 5-dioxide. Recently, Gilman and Esmay (651,755) prepared the oxide in excellent yields (79%) by the controlled oxidation of dibenzothiophene with hydrogen peroxide. Using slightly different conditions, Schlesinger and Mowry obtained a 55% yield of the monooxide (724). The preparation of dibenzothiophene 5-oxide by controlled oxidation of the thiophene with sodium dichromate and acetic acid has also been reported (92).

Dibenzothiophene 5-oxide can be readily reduced. An 85% conversion of oxide to the corresponding thiophene can be effected with stannous chloride and hydrochloric acid (69). Reduction with as mild a reducing agent as ethylmagnesium bromide has also been reported (117).

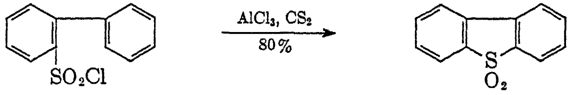
Dibenzothiophene 5-dioxide was first prepared by Stenhouse (489) by the oxidation of dibenzothiophene with potassium dichromate. Since he had already considered dibenzothiophene to be an isomer of diphenyl sulfide, he assumed that he had obtained the sulfone of that isomer. Graebe (247) also prepared this sulfone and, as in the case of dibenzothiophene, assigned the correct structure to this material.

Dibenzothiophene 5-dioxide can be prepared in excellent yields by the oxidation of dibenzothiophene with either hydrogen peroxide (239,755,292) or chromic acid (92,77) (eq. 24).



(24)

Other methods used to prepare the sulfone involve the cyclization of biphenyl-2-sulfonyl chloride (92) and the deamination of benzidine sulfone (136,250,123) (eqs. 25 and 26). The latter transformation was used to corroborate the theory that fuming sulfuric acid cyclized benzidine to a dibenzothiophene derivative.



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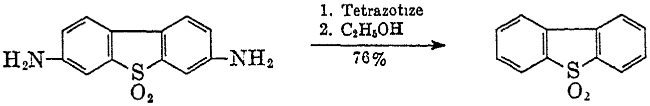
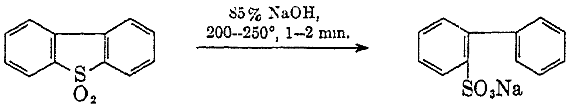


(26)

Until recently, the successful reduction of dibenzothiophene 5-dioxide had not been reported. Treatment of the dioxide with molten sulfur does afford fair yields of the thiophene, but as mentioned previously this is a replacement rather than a simple reduction reaction (see eq. 9). Reduction of the dioxide has been accomplished in good yields with lithium aluminum hydride (see eq. 11).

Fusion of dibenzothiophene 5-dioxide with alkali cleaves the thiophene ring and produces 2-hydroxybiphenyl (118). When this reaction is run under less vigorous conditions, the intermediate biphenyl-2-sulfonic acid can be isolated (122) (eq. 27). Both of these reactions have been used in



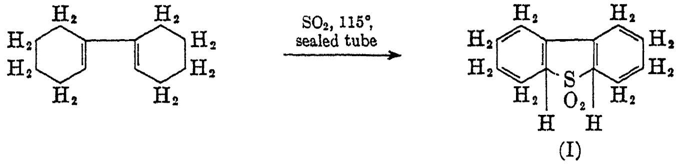
(27)

determining the positions of various groups on substituted dibenzothiophenes.

Treatment of both dibenzothiophene 5-oxide and dibenzothiophene 5-dioxide with Raney nickel gave products which could not be identified (651).

The sulfone of 2,8-dimethyldibenzothiophene has been reported (224). As mentioned previously, the alkyl groups were assigned the 1,9-positions. It seems more probable, however, that they are substituted at the 2,8-positions.

1,2,3,4,4a,5a,6,7,8,9-Decahydrodibenzothiophene 5-dioxide (I) has been made by a Diels-Alder type reaction (252,28) (eq. 28). I decomposes rapidly at temperatures of 110–120°. It reacts with bromine to form an addition product which can be dehydrobrominated to an octahydrodibenzothiophene 5-dioxide (II) of unknown structure (eq. 29). II melts sharply at 165.5 to 166.5° and is presumably a pure material. It forms a dibromide, m.p. 172–173.5°. Ozonization of II yields a small amount of adipic acid. The hydrogenation of I over palladium or platinum oxide leads to the dodecahydrodibenzothiophene 5-dioxide (57).



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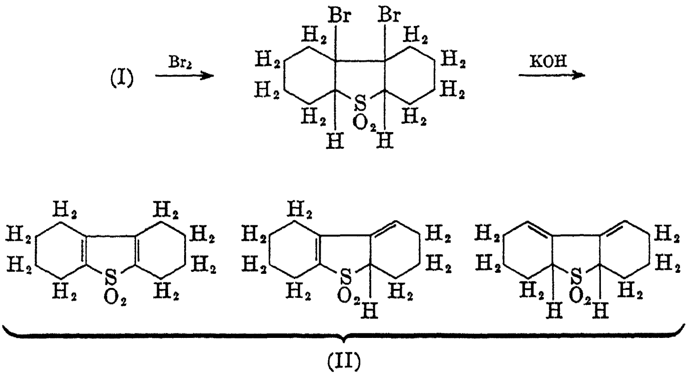

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TABLE IV-2. Melting Points of Oxides of Dibenzothiophene and Their Hydro and Alkyl Derivatives

Derivative	M.p., °C.	Ref
5-Oxide	188–188.5	117
	186	92
	185–187	69
	175	392
5-Dioxide	235	136
	233–234	239
	232–232.5	123
	230	247,489,77
	228	250,392
2,8(?)-Dimethyl 5-dioxide	287–288	224
1,2,3,4,6,7,8,9-Octahydro 5-dioxide	84–85	684
Octahydro 5-dioxide	165.5–166.5	28
1,2,3,4,4a,5a,6,7,8,9-Decahydro 5-dioxide	76–77	253
	78–78.5	28
1,2,3,4,4a,5a,6,7,8,9,9a,9b-Dodecahydro 5-dioxide	85–86 B.p. 173–175 (6 mm.)	57

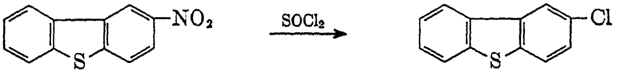
V. Halogen Derivatives

A. Chlorodibenzothiophenes

High temperature chlorination or catalytic chlorination of dibenzothiophene has not been reported. The direct chlorination of dibenzothiophene at low temperatures yields dibenzothiophene 5-dichloride (69). This material was not isolated, but immediately hydrolyzed at 0° to dibenzothiophene 5-oxide.

It would be interesting to study the thermal decomposition of dibenzothiophene 5-dichloride to determine whether migration of chlorine to the nucleus occurs. The heating of dibenzoselenophene 5-dichloride yields 2-chlorodibenzoselenophene (39).

2-Chlorodibenzothiophene has been prepared in good yields by an unusual reaction (119,327) (eq. 30). This replacement does not occur with 2-nitrodibenzofuran (134). Several investigators have reported the replacement of nitro groups by chlorine atoms in the benzene (670), biphenyl (671), and naphthalene series (672). Apparently, more than direct replacement is involved in this reaction, since sulfuryl chloride, which is not a reducing agent, does not cause a similar replacement (672). The inorganic products of this reaction do not seem to have been investigated.

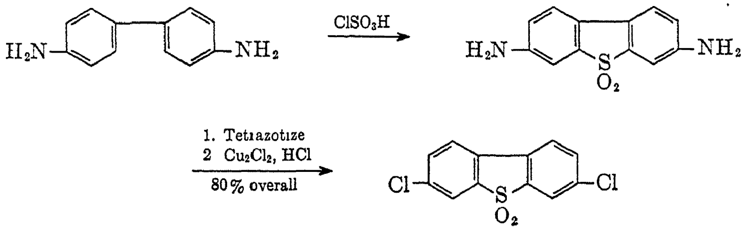


(30)

2-Chlorodibenzothiophene has also been prepared from 2-aminodibenzothiophene by the Sandmeyer reaction (119,127). It can be oxidized with either hydrogen peroxide or potassium dichromate and acetic anhydride to 2-chlorodibenzothiophene 5-dioxide (127). This sulfone has also been made by the cyclization of 5-chlorobiphenyl-2-sulfonyl chloride with aluminum chloride (127,94).

2,8-Dichlorodibenzothiophene has been made by means of the Sandmeyer reaction from the corresponding 2,8-diamino derivative. This dichloro derivative can also be oxidized by hydrogen peroxide to the sulfone (127).

The sulfonation of 4,4′-dichlorobiphenyl leads directly to the formation of 3,7-dichlorodibenzothiophene 5-dioxide (127). Much better yields of this material are obtained by cyclizing benzidine with chlorosulfonic acid, followed by replacement of the amino groups by chloro groups (eq. 31). Alkali fusion of this material followed by acidification yields 4,4′-dichlorobiphenyl-2-sulfonic acid (eq. 32). If the alkali fusion is carried out under more drastic conditions, 4,4′-dichloro-2-hydroxybiphenyl is obtained.



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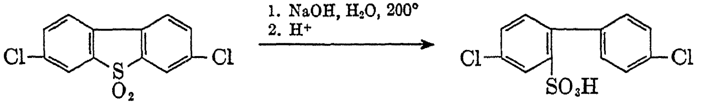

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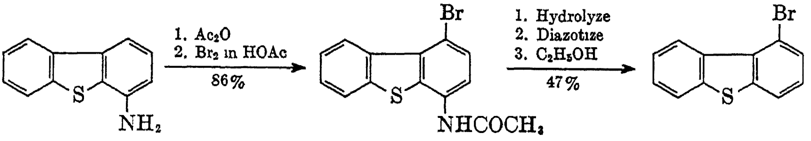
B. Bromodibenzothiophenes

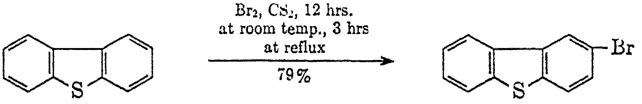
1-Bromodibenzothiophene has been made from 4-aminodibenzothiophene by the following series of reactions (231) (eq. 33). It seems to be



(33)

generally true that, when a ring activating group is present in the 4-position, substitution at the 1-position occurs. However, there are insufficient examples of this type of substitution to establish this rule with certainty. Oxidation of the 1-bromodibenzothiophene with sodium dichromate in acetic acid containing trace amounts of sulfuric acid yields the sulfone.

2-Bromodibenzothiophene can be made by the direct bromination of dibenzothiophene (135,119,127,P-230) (eq. 34). Chloroform and carbon bisulfide are the usual solvents for this reaction. The halides of trivalent metals and iron powder have been used to catalyze this reaction (P-605).



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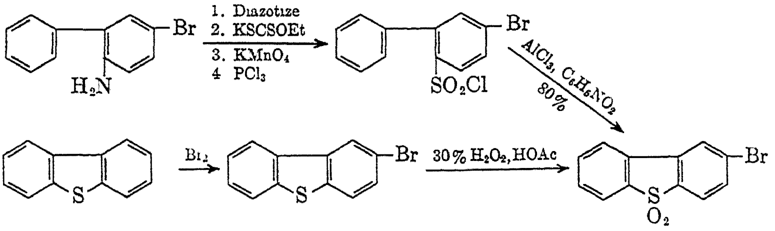
Unequivocal proof of the position occupied by the bromine atom has been achieved by the reactions illustrated in eq. 35 (94).



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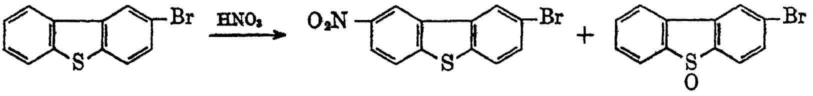
Recently, the reaction of *N*-bromosuccinimide with dibenzothiophene has been reported to yield the 2-bromo derivative in poor yields (83). This is in marked contrast to the good yields obtained with dibenzofuran.

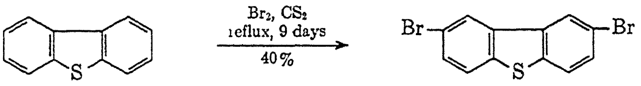
Other syntheses of 2-bromodibenzothiophene involve replacement of the amino group by means of the Sandmeyer reaction (135,119,127) and the action of thionyl bromide on 2-nitrodibenzothiophene (119).

2-Bromodibenzothiophene 5-oxide has been prepared by the oxidation of 2-bromodibenzothiophene with limited amounts of 30% hydrogen peroxide (392). The oxide is also formed as a by-product in the nitration of 2-bromodibenzothiophene (119) (eq. 36). The methods for formation of the dioxide have been mentioned previously.



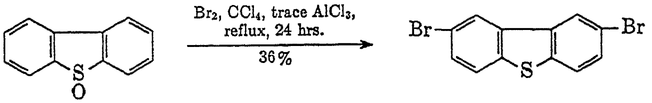
(36)

2,8-Dibromodibenzothiophene can be made by direct bromination of dibenzothiophene (396,119). Iron powder has been used as a catalyst for this reaction (P-605,651) (eq. 37). This compound has also been synthesized from the diamino derivative via the Sandmeyer reaction (119, 127).



(37)

The direct bromination of dibenzothiophene 5-oxide yields 2,8-dibromodibenzothiophene without any observable evolution of hydrogen bromide (673,731) (eq. 38). This is rather surprising since substitution of the sulfoxide normally involves the 3- and 3,7-positions. A possible explanation for this reaction involves a chain-type mechanism (eqs. 39 and 40).



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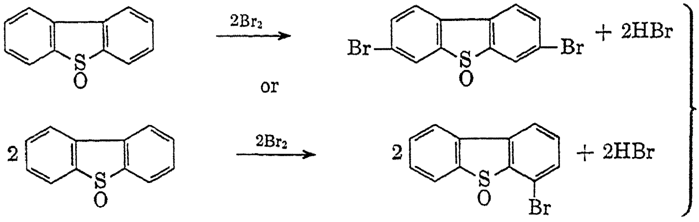

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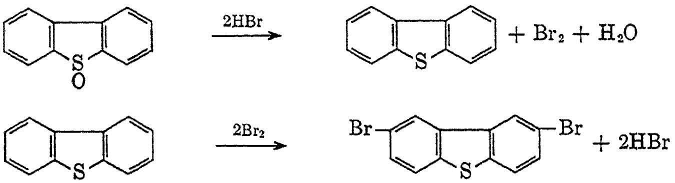
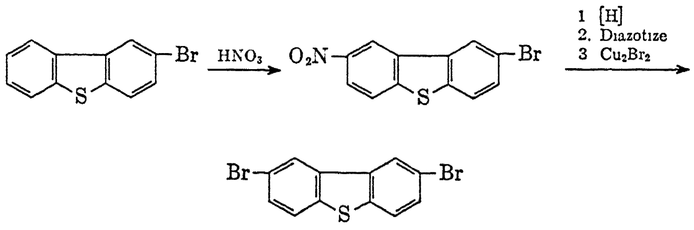


(40)

Hydrogen bromide is generated in the initiation step which then reduces the sulfoxide to the thiophene. The dibenzothiophene is then dibrominated with the evolution of hydrogen bromide which continues the chain reaction.

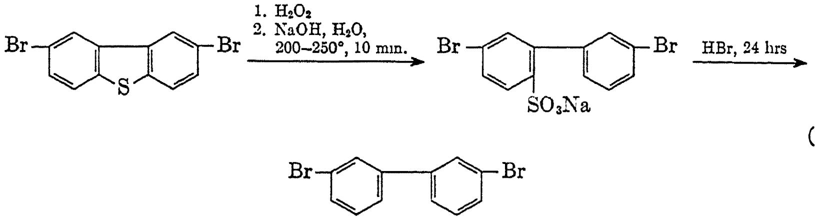
2-Bromodibenzothiophene can be converted to the 2,8-dibromo derivative (eq. 41). It is interesting to note that the bromination of 2-nitrodibenzothiophene yields the same material that is obtained from the nitration



(41)

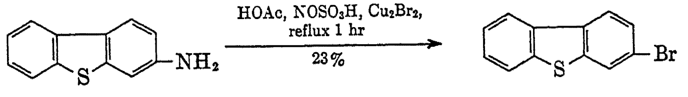
of 2-bromodibenzothiophene (126). Therefore, it was concluded that both bromine atoms must occupy identical positions with respect to the sulfur and the biphenylene linkage. Since the first bromine atom had been shown to occupy the 2-position, the disubstituted material must be the 2,8-derivative. It is a general rule that electrophilic reactions involving disubstitution of dibenzothiophene yield the 2,8-derivatives.

A more rigorous proof of the structure of 2,8-dibromodibenzothiophene was carried out by Courtot and Chaix (122) (eq. 42). Fusion of 2,8-dibromodibenzothiophene 5-dioxide with sodium hydroxide containing a small amount of water yields sodium 3,3′-dibromodiphenyl-6-sulfonate. Treatment of this material with hydrobromic acid leads to the formation of 3,3′-dibromobiphenyl. Courtot had expected to obtain the 4,4′-dibromobiphenyl, since, prior to this work, he believed that mono- and disubstitution occurred at the 3- and 3,7-positions, respectively (118). A number of the derivatives reported by Courtot previous to this time have incorrectly assigned structures.



(42)

3-Bromodibenzothiophene has been synthesized from the 3-amino derivative via the Sandmeyer reaction (657) (eq. 43). This material can also be prepared by the bromination of 2-acetamidodibenzothiophene followed by deamination (240) (eq. 44). The acetamido group directs the incoming



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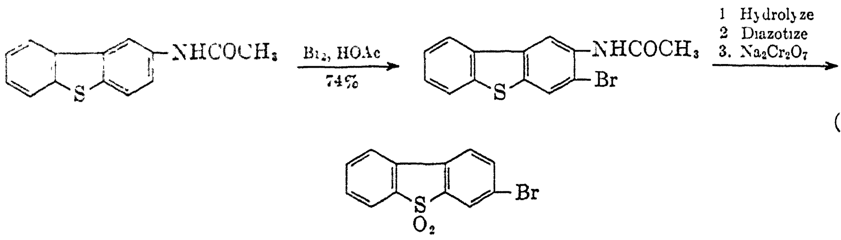


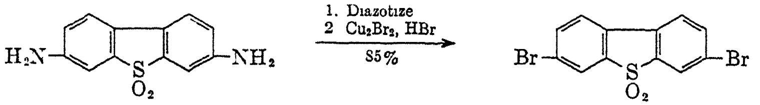
(44)

bromine atom to the 3-position. The 3-bromodibenzothiophene was not isolated in this case, but was converted immediately to the dioxide for purposes of identification.

3-Bromodibenzothiophene 5-dioxide has also been made from dibenzothiophene 5-dioxide by nitration followed by conversion of the nitro group to a bromo group (232). All attempts to reduce this material to the thiophene were unsuccessful.

An attempt to prepare 3,7-dibromodibenzothiophene by the reaction of sulfur with *p,p′*-dibromobiphenyl in the presence of aluminum chloride was unsuccessful, yielding only dibenzothiophene (648).

3,7-Dibromodibenzothiophene 5-dioxide can be prepared from 3,7-diaminodibenzothiophene 5-dioxide (benzidine sulfone) (121,135) (eq. 45).



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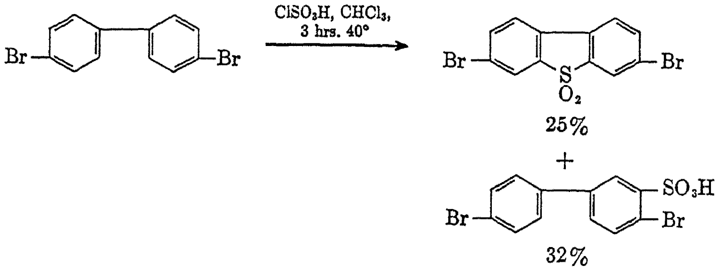
3,7-Dibromodibenzothiophene 5-dioxide can also be prepared directly by the sulfonation of 4,4′-dibromobiphenyl with fuming sulfuric acid, but the yields are much poorer than those obtained with benzidine sulfone.

The addition of chlorosulfonic acid to 4,4′-dibromobiphenyl yields 3,7-dibromodibenzothiophene 5-dioxide along with considerable quantities of 4,4′-dibromobiphenyl-3-sulfonic acid (123) (eq. 46). When the 4,4′-



(46)

dibromobiphenyl is added to the chlorosulfonic acid, a 42% yield of the sulfone is obtained along with 42% of the 4,4′-dibromobiphenyl-3,3′-disulfonic acid and 13% of the 4,4′-dibromobiphenyl-3,3′-disulfonyl chloride. With 15% oleum, an 18% yield of the sulfone is obtained, while with 30% oleum, only 2,8-disulfo-3,7-dibromodibenzothiophene 5-dioxide could be isolated.

3,7-Dibromodibenzothiophene 5-dioxide has also been made by the direct bromination of dibenzothiophene 5-dioxide (135). Since this material was identical to the one formed from benzidine sulfone, it proved conclusively that dibromination of the sulfone leads to the 3,7-derivative.

4-Bromodibenzothiophene has been made by the bromination of 4-dibenzothienyllithium. However, the 4-bromodibenzothiophene was not purified and was used in subsequent reactions.

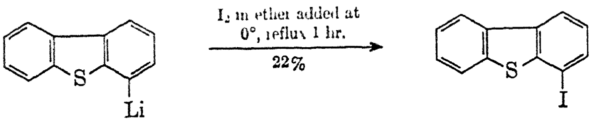
C. Iododibenzothiophenes

2-Iododibenzothiophene and 2,8-diiododibenzothiophene have been synthesized from 2-amino- and 2,8-diaminodibenzothiophenes by the Sandmeyer reaction (119).

TABLE IV-3. Melting Points of Halogenated Dibenzothiophenes and Their Derivatives

			5-Dioxide	
Substituent	M.p., °C.	Ref.	M.p., °C.	Ref.
2-Cl	113–114	119,127	249	127,94
2,8-Di-Cl	212	127	340	127
	205–206	119		
3,7-Di-Cl	—	—	295–296	121
1-Br	84	231	171	232
2-Br	126–127	119,127,P-230	266–267	127
		135,83	263	94
			256	392
2-Br-5-oxide	171–172	392,119		
2,8-Di-Br	229	119	361–362	127
	225–226	651	360–361	651
	225–228	396	341–344	396,P-695
	223–224	673,731		
3-Br	97–98.5	657,734	224–225	232,240,734
3,7-Di-Br	—	—	315	123
			312–313	121,135
4-Br	Not listed	231		
2-I	87–88	119		
4-I	101–102 B.p. 160–170 (10 mm.)	239		
2,8-Di-I	219–220	119		

4-Iododibenzothiophene has been made by the action of iodine on 4-dibenzothienyllithium (239) (eq. 47). When 4-iododibenzothiophene is treated with sodamide, a rearrangement takes place and 3-aminodibenzothiophene is obtained. To show that rearrangement did not occur during metalation, it was necessary to metalate the iodo compound and carbonate it to form the known 4-acid.



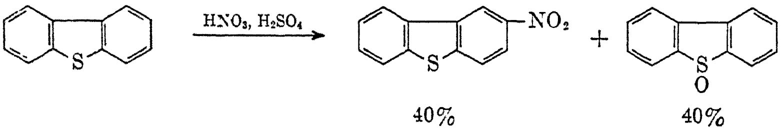
(47)

VI. Nitrogen Derivatives

A. Nitrodibenzothiophenes

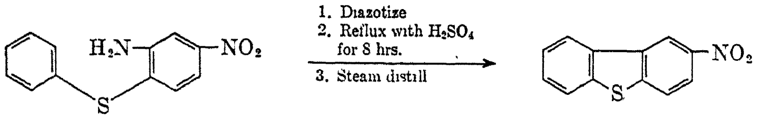
Direct nitration of dibenzothiophene yields exclusively the 2-isomer which is in accordance with other electrophilic substitutions of dibenzothiophene. However, the exclusive isolation of only the 2-isomer is surprising, since in the nitration of dibenzofuran the 3-isomer is formed in predominance (655). For further discussion see Chapter I.

Dibenzothiophene reacts with mixed acid to form equal amounts of 2-nitrodibenzothiophene and dibenzothiophene 5-oxide (eq. 48). Mixtures of acetic acid and nitric acid have also been used to nitrate dibenzothiophene, 28–40% yield (242,232). It is surprising to find that even when acetic acid is substituted for the sulfuric acid, the nitro material and the sulfoxide are still formed in identical amounts.



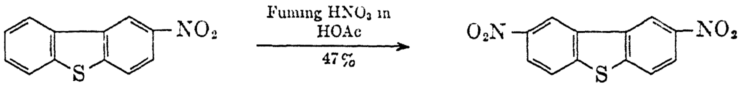
(48)

2-Nitrodibenzothiophene has also been made by cyclizing 2-amino-4-nitrodiphenyl sulfide (135,392) (eq. 49). This method was used to establish the position of the entering nitro group during the direct nitration of dibenzothiophene.



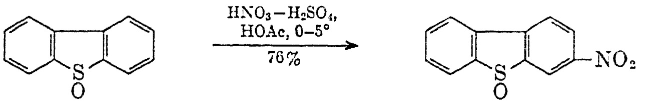
(49)

2,8-Dinitrodibenzothiophene can be made by the nitration of 2-nitrodibenzothiophene (242,117) (eq. 50). Attempts to prepare the dinitro material directly from dibenzothiophene were unsuccessful.



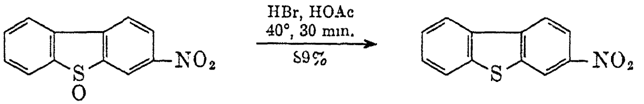
(50)

The direct nitration of the sulfoxides or sulfones of dibenzothiophene leads exclusively to the 3-isomers. 3-Nitrodibenzothiophene 5-oxide has been prepared in high yields by the nitration of dibenzothiophene 5-oxide (69,392) (eq. 51).



(51)

Reduction of the oxide with hydrobromic acid yields 3-nitrodibenzothiophene (740) (eq. 52). The oxide can also be reduced with a stannous



(52)

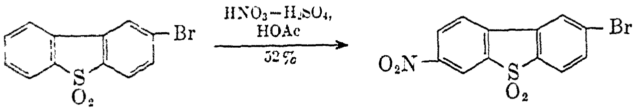
chloride-concentrated hydrochloric acid mixture to 3-nitrodibenzothiophene in 35% yield. It is imperative that the reaction temperature be kept below 40° or further reduction to the amine will occur.

The nitration of either dibenzothiophene 5-oxide or 3-nitrodibenzothiophene 5-oxide with mixed acid at temperatures of 10–15° gives 3,7-dinitrodibenzothiophene 5-oxide in good yields (740). Its structure was confirmed by oxidizing it to the known 3,7-dinitrodibenzothiophene 5-dioxide. Reduction of the 3,7-dinitrodibenzothiophene 5-oxide with hydrobromic acid gives an excellent yield of 3,7-dinitrodibenzothiophene. This material can be oxidized quantitatively to the sulfone.

The nitration of dibenzothiophene 5-dioxide under controlled conditions leads to an 82% yield of 3-nitrodibenzothiophene 5-dioxide (232). This sulfone has also been prepared by oxidation of the corresponding sulfoxide (69). The dinitration of dibenzothiophene 5-dioxide yields the 3,7-derivative (135,232). The structure of this material was conclusively established by reducing it to the well-known 3,7-diaminodibenzothiophene 5-dioxide (benzidine sulfone).

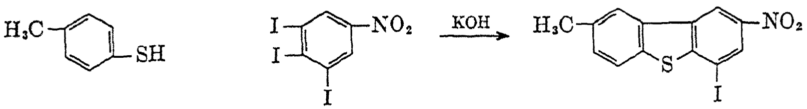
2-Bromodibenzothiophene can be nitrated to yield 2-nitro-8-bromodibenzothiophene (119,126). The position of the entering nitro group was established by conversion of the material to 2,8-dibromodibenzothiophene.

The nitration of 2-bromodibenzothiophene 5-dioxide yields a mononitro derivative which is probably 2-bromo-7-nitrodibenzothiophene 5-dioxide (650) (eq. 53). Although the structure of this material was not conclusively proved, it appears, on the basis of other reactions of sulfones and the presumable deactivating effect of the bromine groups, that this is the correct isomer. 2,8-Dibromodibenzothiophene has been nitrated to give a dinitro-2,8-dibromodibenzothiophene of unknown structure (651).



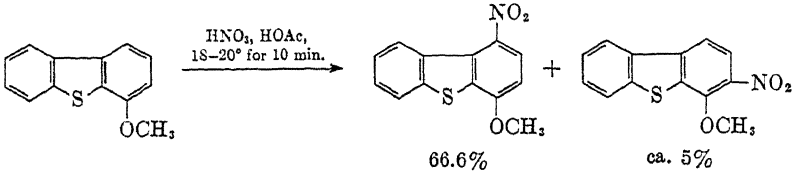
(53)

2-Nitro-4-iodo-8-methyldibenzothiophene has been isolated from the reaction of *p*-thiocresol and 3,4,5-triiodonitrobenzene (654,656) (eq. 54). This reaction has been used to prepare a number of ethoxydibenzothiophenes and will be discussed more thoroughly in that section.



(54)

The nitration of 4-methoxydibenzothiophene yields predominantly 1-nitro-4-methoxydibenzothiophene with minor amounts of a second isomer tentatively assumed to be the 3-isomer (240) (eq. 55). The structure of the first material was assigned on the basis that 4-methoxydibenzofuran is nitrated entirely in the 1-position. As mentioned previously, comparison of the reactions of dibenzofuran and dibenzothiophene, especially with regard to nitration, can be misleading. However, in view of other reactions that have been carried out on 4-substituted dibenzothiophenes, this appears to be the correct conclusion.



(55)

The second derivative was not isolated, but was first reduced and then isolated as the amine. This secondary nitration was assumed to take place at the 3-position.

TABLE IV-4. Melting Points of the Nitrodibenzothiophenes and Their Derivatives

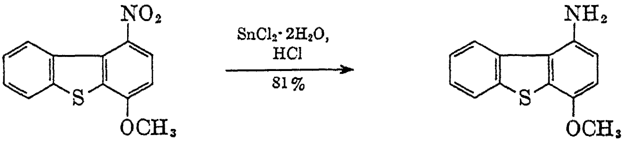
Substituent	M.p., °C.	Ref	5-Dioxide	
			M.p., °C.	Ref.
$2\text{-}NO_2$	186–187	242,135,392	255–256	242
	184	117,119	254	392
			258	135,740
$2,8\text{-Di-}NO_2$	339–340	242		
	324–325	217		
$2\text{-}NO_2\text{-}8\text{-Br}$	264	119		
$2\text{-}NO_2\text{-}4\text{-I-}8\text{-}CH_3$	270	656,654		
$3\text{-}NO_2$	153–154	740	265–266	232,239,69
$3\text{-}NO_2\text{-}5\text{-oxide}$	212	392		
	209.5–210.5	69		
$3,7\text{-Di-}NO_2$	354–356	740	290	135,232
			283–285	740
$3,7\text{-Di-}NO_2\text{-}5\text{-oxide}$	267–268	740		
$7\text{-}NO_2\text{-}2\text{-Br}$	—	—	319–321	649
$\text{Di-}NO_2\text{-}2,8\text{-di-Br}$	310–311	651		

B. Aminodibenzothiophenes

1. Nuclear Amino Groups

1-Aminodibenzothiophene is unknown. It could probably be synthesized from 4-acetamidodibenzothiophene as follows: (*1*) nitration; (*2*) hydrolysis of the acetamido group followed by removal of the $—NH_2$ group; (*3*) reduction of the 1-nitro derivative. An alternative synthesis from 1-bromodibenzothiophene would involve direct replacement of the bromo group with ammonia (see 2-amino derivative below).

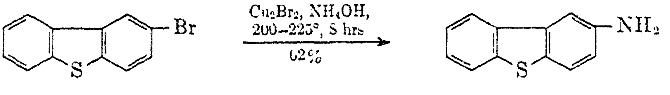
The 4-methoxy derivative of 1-aminodibenzothiophene has been prepared by reduction of the corresponding nitro material (240) (eq. 56).



(56)

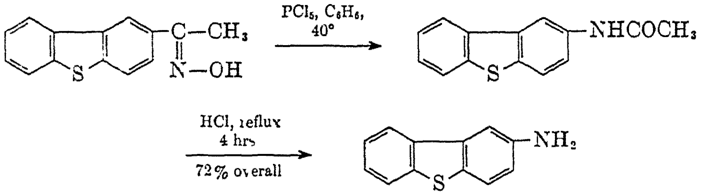
2-Aminodibenzothiophene is normally prepared by reduction of the 2-nitro derivative. The best yield (91%) is obtained by catalytic hydrogenation employing Raney nickel catalyst (242). Other reduction methods, similar in most respects to those used for the reduction of nitrobenzene, employed zinc and alcoholic ammonia (117,119,135), iron filings and water (135), and tin and hydrochloric acid (242). Inferior yields and an impure product are obtained by the latter methods.

2-Aminodibenzothiophene has also been made from the 2-bromo derivative by reacting it with ammonium hydroxide in the presence of copper salts (231,392) (eq. 57). This method appears to lead to the best yields based on dibenzothiophene as a starting material.



(57)

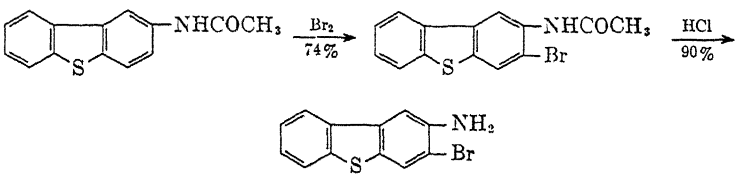
A number of investigators have reported the formation of 2-acetamidodibenzothiophene by the Beckmann rearrangement of the oxime of 2-acetyldibenzothiophene (71,242,231). The amide can be easily hydrolyzed to the amine (eq. 58). The toxicological activity of the amide toward rats has been reported recently (685).



(58)

2-Aminodibenzothiophene 5-dioxide has been prepared by the reduction of the corresponding nitro derivative with hydrogen sulfide in pyridine (392), with tin and hydrochloric acid (59% yield) (242), and with a stannous chloride-hydrochloric acid mixture in almost quantitative yield (740).

2-Amino-3-bromodibenzothiophene has been made by the bromination of the 2-acetamidodibenzothiophene followed by acid hydrolysis (240) (eq. 59). The position of the entering bromine atom was proved by converting the above material to the known 3-bromodibenzothiophene 5-dioxide. The chloro derivative can be made in a similar fashion using sulfuryl chloride as the chlorinating agent.

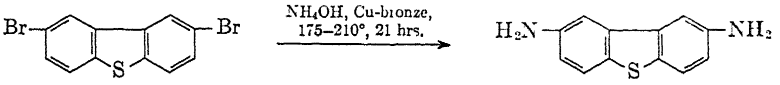


(59)

The nitration of 2-acetamidodibenzothiophene with fuming nitric acid leads to a 67% yield of a material which analyzes as a nitro-2-acetamidodibenzothiophene and a 3–4% yield of nitroaminodibenzothiophene (231). Hydrolysis of the amide yielded a product, m.p. 88°, which did not contain nitrogen. The structure of this nitrogen-free material was not determined.

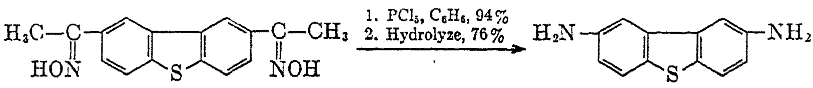
The reduction of 2,8-dinitrodibenzothiophene over Raney-nickel catalyst gives a 46% yield of the pure amino derivative (242). Chemical reduction with tin and hydrochloric acid affords only a 35% yield of impure material (242,117).

The diamino derivative can also be synthesized by reacting 2,8-dibromodibenzothiophene with ammonium hydroxide (396) (eq. 60).



(60)

The Beckmann rearrangement of the dioxime of 2,8-diacetyldibenzothiophene followed by subsequent hydrolysis also yields the diamino derivative (71,242). On the basis of reported yields, this appears to be the best method for preparing 2,8-diaminodibenzothiophene. However,



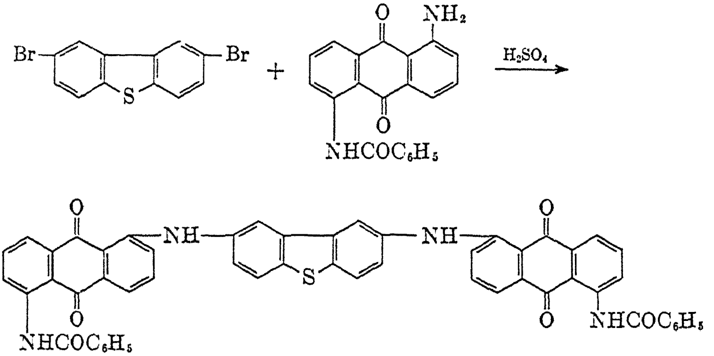
(61)

Neumoyer and Amschutz (396) have reported that the reaction of the dibromo material with ammonia is a much more satisfactory method for preparing sizable amounts of material. No yield data were given.

It should be noted that the improperly assigned positions of the amino groups in 2,8-diaminodibenzothiophene contributed greatly to the early confusion which existed with regard to the orientation of dibenzothiophene substituents (118). Courtot and Pomonis obtained from the dinitration and reduction of dibenzothiophene an amine which they assumed to be substituted in the 3,7-positions for the following reasons. The amine was acetylated and oxidized to the sulfone. Alkali fusion gave a material which they identified as 2-hydroxy-4,4′-diaminobiphenyl. This material could have only come from a dibenzothiophene substituted in the 3,7-positions. This mistake was later corrected by Courtot and Chaix (122). However, no mention was made of the structure of the substituted biphenyl, previously obtained by alkali fusion, and it must be presumed that the material was actually 6-hydroxy-3,3′-diaminobiphenyl and not 2-hydroxy-4,4′diaminobiphenyl as previously believed.

A number of dyes which are derivatives of 2-amino- and 2,8-diaminodibenzothiophene have been prepared. A British patent (P-137) lists the preparation of azo dyes of 2-amino-3-nitrodibenzothiophene and its sulfone. However, neither the preparation nor the physical constants of the starting materials are given.

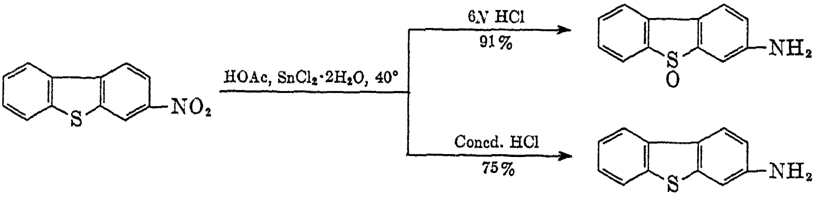
Dyes of the following type have been made by condensing 2,8-dibromodibenzothiophene or its dioxide with aminoanthraquinones (P-252) (eq. 62).



(62)

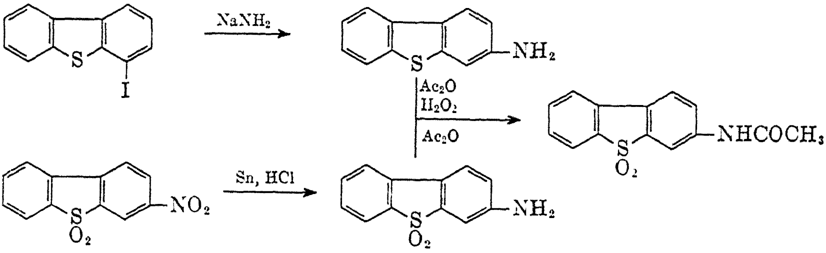
These dyes are brown-violet powders, very difficult to vat, and dye cotton brown-red to violet.

The nitration of dibenzothiophene 5-oxide leads to the 3-nitro derivative which can be reduced to 3-aminodibenzothiophene by a variety of methods. As is shown by the following equation, reduction in concentrated hydrochloric acid results in reduction of both the nitro and sulfoxide groups, while reduction in dilute hydrochloric acid leads only to the reduction of the nitro group (69) (eq. 63). The reduction of 3-nitrodibenzothiophene 5-oxide with hydrogen sulfide and pyridine yields 3-aminodibenzothiophene 5-oxide (392). This can be further reduced to the thiophene by zinc dust and alcohol.



(63)

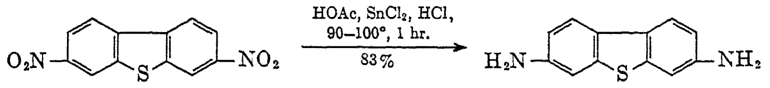
The 3-position has been made further accessible by the interesting reaction reported by Gilman and Nobis (239). The reaction of 4-iododibenzothiophene with sodamide yields 3-aminodibenzothiophene rather than the expected 4-derivative. The structure of the 3-aminodibenzothiophene was established by conversion to the known 3-acetamidodibenzothiophene 5-dioxide (eq. 64). 3-Acetamidodibenzothiophene 5-dioxide has also been prepared by the oxidation of 3-acetamidodibenzothiophene 5-oxide (69).



(64)

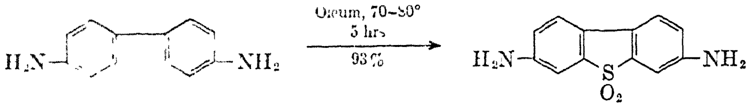
The carcinogenic activity of 3-acetomidodibenzothiophene and its 5-oxide was compared with that of 2-acetamidofluorene in male and female rats (635). Replacement of the CH_2 bridge in fluorene by sulfur produced no change in carcinogenicity for mammary gland or earduct tissues. Substitution of a sulfoxide group for the CH_2 bridge caused a considerable decrease in activity. 3-Acetamidodibenzofuran is slightly less active than its thiophene analog but more effective than the sulfoxide. Of the four materials, only 3-acetamidofluorene displayed any carcinogenic activity toward the liver.

3,7-Diaminodibenzothiophene has been synthesized by the reduction of the corresponding nitro derivative (740) (eq. 65). The earlier literature reports that the reaction of sulfur and benzidine yields a material which was called "thiobenzidine" (516,P-669). This material undoubtedly contained some 3,7-diaminodibenzothiophene. However, analyses and melting points indicate that the material was not obtained in the pure form. It is significant to note that by varying the amount of sulfur in the above reaction, "thiobenzidines" of different composition can be obtained. These sulfurized benzidines can be tetrazotized and coupled to form dyes.



(65)

3,7-Diaminodibenzothiophene 5-dioxide (benzidine sulfone) has been made by a variety of methods. The most general method consists of cyclizing benzidine with fuming sulfuric acid (136,120) (eq. 66). The amine groups can be removed and dibenzothiophene 5-dioxide is obtained.



(66)

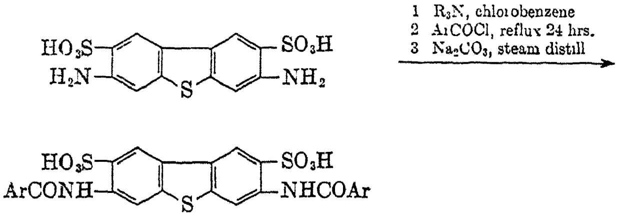
Griess and Duisberg (250), who originally made the benzidine sulfone, were able to convert it to a diaminohydroxybiphenyl. This was probably 4,4′-diamino-2-hydroxybiphenyl which Courtot and Pomonis (118) thought they had obtained from their diamine derivative. Unfortunately, Griess and Duisberg listed no melting point.

Benzidine sulfone has also been prepared in high yields by the action of ammonia on 3,7-dibromodibenzothiophene 5-dioxide (123). Direct nitration of dibenzothiophene 5-dioxide gives the 3,7-dinitro derivative which can be reduced easily to the benzidine sulfone (135,740).

The reaction of benzidine sulfone and Raney nickel during *N*-alkylation yields bis-3,3′-*N*,*N*′-ethylaminobiphenyl (683).

There are a number of articles and patents relating to the conversion of benzidine sulfone to dye compositions (P-264,P-157,145,P-265,P-266). The sulfones can be either tetrazotized and coupled, or sulfonated and then tetrazotized and coupled Other dye materials can be obtained by oxidizing the amine sulfonic acid to the azoxy material (531,532) and by coupling these benzidinesulfonedisulfonic acids with aldehydes to form Schiff bases (397). The positions of the sulfonic groups have not been established, but it was believed that they had entered the 2,8-positions. As far as can be ascertained from the literature, it seems that none of these dyes ever attained commercial importance.

It has been recently disclosed that acylated derivatives of materials such as 3,6-diamino-2,8-disulfodibenzothiophene 5-dioxide are excellent optical bleaching and brightening agents (P-712,P-709,P-711) (eq. 67).

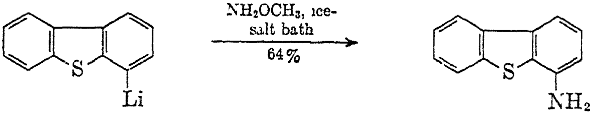


(67)

The acylation step is greatly facilitated if the sulfonic acid is initially neutralized by a tertiary amine (P-709,P-710).

A recent patent describes the preparation of dialkyldiaminodibenzothiophenes by the nitration of dialkyldibenzothiophenes followed by reduction (P-690). No pure compounds were isolated, but it appears that these mixtures probably contain predominant amounts of 2,8-dialkyl-3,7-diaminodibenzothiophenes. Incorporation of small amounts of these materials in lubricating oils is said to improve their stability toward oxidation.

4-Aminodibenzothiophene has been prepared in good yields by the reaction of 4-dibenzothienyllithium with *O*-methylhydroxylamine (240) (eq. 68). It has also been prepared in 25% yield from 4-hydroxydibenzothiophene by means of the Bucherer reaction, in 35% yield by the amination of 4-bromodibenzothiophene and in 48% yield from 4-dibenzothiophenecarboxylic acid amide via the Hoffmann reaction (651,755).

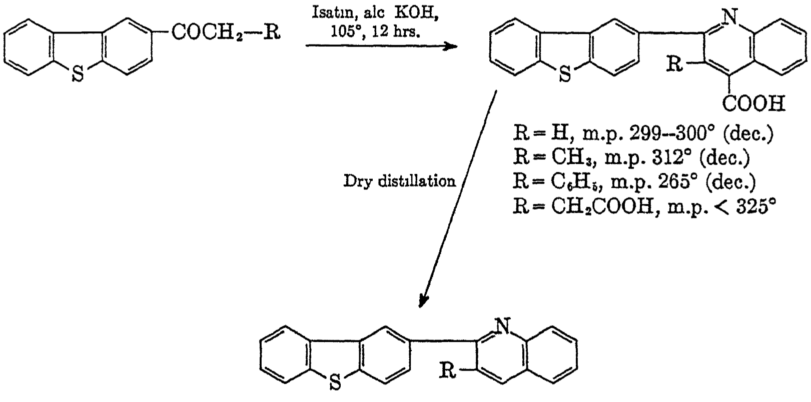


(68)

The only nuclear-substituted 4-aminodibenzothiophene that has been reported is the 1-bromo derivative. This material has been made by bromination of 4-acetamidodibenzothiophene followed by hydrolysis (231).

2. *Side Chain Amino Groups*

2-Acyldibenzothiophenes undergo the Pfitzinger reaction with isatin forming 3′-substituted 2-(4′-carboxy-2′-quinolyl)dibenzothiophenes (488, 80,83,77). Decarboxylation of the cinchoninic acid yields the quinolyldibenzothiophene (eq. 69). Attempts to make 2-heptanoyldibenzothio-



R = H, m.p. 299–300° (dec.)
R = CH_3, m.p. 312° (dec.)
R = C_6H_5, m.p. 265° (dec.)
R = CH_2COOH, m.p. < 325°

(69)

R = H, m.p. 144–145°
R = CH_3, m.p. 149°; picrate, m.p. 235–236° (dec.)
R = C_6H_5, m.p. 206°; picrate, m.p. 247–249° (dec.)

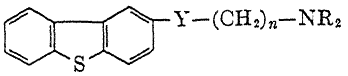
TABLE IV-5. Physical Constants of Aminodibenzothiophenes and Their Derivatives

Substituents	M.p., °C.	Ref.	Acetamido Deriv., m p. °C.,	Ref.
1-NH_2-4-OCH_3	101–102	240		
1-$NH(CH_2)_3N(C_2H_5)_2$-4-OCH_3	B.p. 251–255 (0.15 mm.)	240		
2-NH_2	131–133	119,71,117	181–183	71
		135,392	178	117
	129–131	242	167–168	231
	129	231		
2-NH_2-5-dioxide	278–280	242,740	273–274	740
	265	392		
2,8-Di-NH_2	200–201	396,242	303–305	396,242
	194	71	253–255	71
	177–178	117,118,P-690	237–239	117
2,8-Di-NH_2-5-dioxide	327–328	242	356–357	242
	329–331	396,P-695	378	117
2-NH_2-3-Cl	118–119	240	199.5–200	240
2-NH_2-3-Br	135–135.5	240	199–200	240
2-NH_2-3(?)-NO_2	248–250	231	208.5–209	231
2-$NH(CH_2)_3N(C_2H_5)_2$	B.p. 280–282 (2 mm.)	240		
2-$NH(CH_2)_3N(C_2H_5)_2$-3-Cl	B.p. 215–220 (0.11 mm.)	240		
2-$NH(CH_2)_3N(C_2H_5)_2$-3-Br	B.p. 275–280 (0.5 mm.)	240		
3-NH_2	121–123	69,239,392	196–197	69
			199–200	239
			198–199	635

Substituents	M.p., °C.	Ref.	Acetamido deriv., m.p., °C.	Ref.
3-NH_2-5-oxide	208–209	69	265–267	69
	252–253	392	275–276	636
3-NH_2-5-dioxide	259–260	232	322–324	69,232
3,7-Di-NH_2	172–173	740		
	265–270 (?)	516		
3,7-Di-NH_2-5-dioxide	330–332	740		
	327–328	123,126	406–407	123
		135,120	Benzoyl deriv.	
			413–414	123
	>350	250		
3-NH_2-4-OCH_3	132–133	240		
3-NH_2-7-N=CHC_6H_5-5-dioxide	259–260	512		
3,7-Di-NHC_6H_5-5-dioxide	>300	309		
3,7-Di(*p*-$NO_2C_6H_4CH$=N)-5-dioxide	302–304	512		
3,7-Di(*p*-$(CH_3)_2NC_6H_4CH$=N)-5-dioxide	318	512		
4-NH_2	110	231,240,755	195–197	72
			198	231
4-NH_2-1-Br	156	231	254	231
4-$NH(CH_2)_3N(C_2H_5)_2$	B.p. 210–213 (0.11 mm.)	240		
4-$NH(CH_2)_3N$-$(C_2H_5)_2$-1-Br	B.p. 263–266 (0 3 mm.)	240		
7-NH_2-2-Br-5-dioxide	331–333	649		

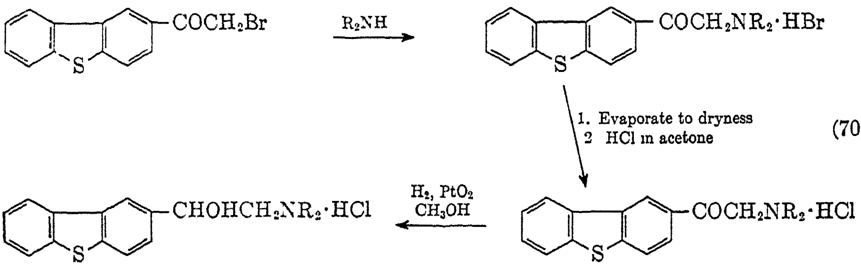
phene undergo the Pfitzinger reaction were unsuccessful. 2,8-Diacetyldibenzothiophene does undergo this reaction to form the dicinchoninic acid, m.p. 330–340° (dec.), which can also be decarboxylated to the bis-2,8-(2′-quinolyl)dibenzothiophene, m.p. 206–207° (488).

A large number of amines of dibenzothiophene, having the following type structures have been synthesized and the analgesic activities of a number of them have been determined (73,72,74). The α-aminoketones



Y = CO, CHOH, CHOOCCH$_3$ and COO
n = 1 or 2
—NR$_2$ = *sec*-amino radical

and alcohols were synthesized as illustrated in eq. 70. The β-aminoketones and alcohols were prepared via the Mannich reaction (eq. 71).



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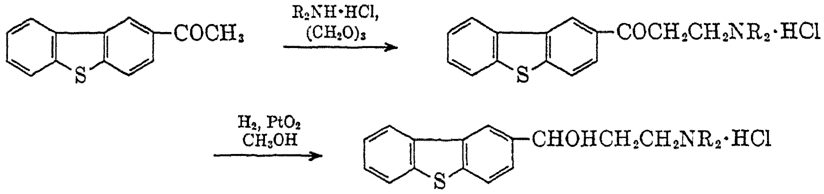


(71)

Fairly good yields were generally obtained for both series of reactions.

When toxic doses of these materials were administered to mice, depression with marked disturbances was noted. With cats, analgesic action was observed. The order of analgesic effectiveness was not the same as the order of toxicity.

The melting points of these compounds and their derivatives are listed in Table IV-6.

TABLE IV–6. Dibenzothiophene Derivatives Having Nitrogen in the Side Chain (73,72,74)

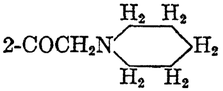
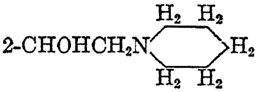
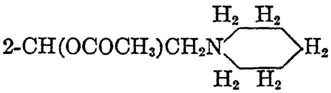
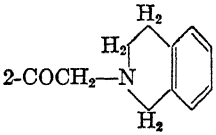
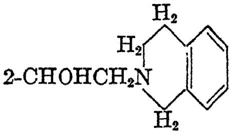
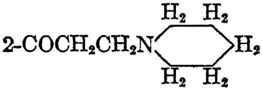
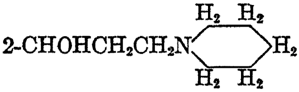
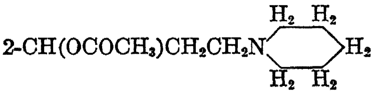
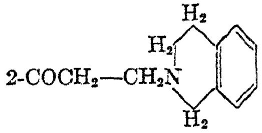
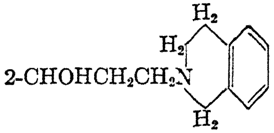
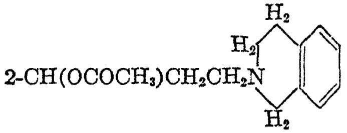
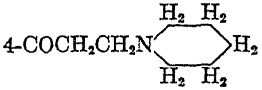
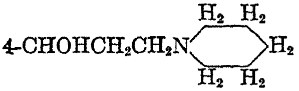
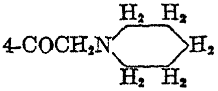
Substituent	M.p., °C.	Derivative	M.p., °C.
2-$COCH_2N(CH_3)_2$	—	HCl	220–225 (dec.)
2-$CHOHCH_2N(CH_3)_2$	—	HCl	228–228 5 (dec.)
2-$CH(OCOCH_3)CH_2N(CH_3)_2$	—	HCl	206–208 (dec.)
2-$COCH_2N(C_2H_5)_2$	—	HCl	214–215
2-$CHOHCH_2N(C_2H_5)_2$	59–60	HCl	163–164
2-$CH(OCOCH_3)CH_2N(C_2H_5)_2$	—	HCl	188–192 (dec.)
	117	HCl	245–246 (dec.)
	88–89	HCl	225–229 (dec.)
	—	HCl	220–225 (dec.)
	— 122–125	HCl HBr	244–246 (dec.) 257–259 (dec.)
	— 106–107	HCl HBr	243–244 (dec.) 250–252
2-$COCH_2CH_2N(CH_3)_2$	—	HCl	192–195 (dec.)
2-$CHOHCH_2CH_2N(CH_3)_2$	118	HCl	137–139
2-$CH(OCOCH_3)CH_2CH_2N(CH_3)_2$	—	HCl	149–150
2-$COCH_2CH_2N(C_2H_5)_2$	—	HCl	150–151
	—	HCl	201–203 (dec.)
	102	HCl	201–201.5 (dec.)
	—	HCl	185–186

Table continued

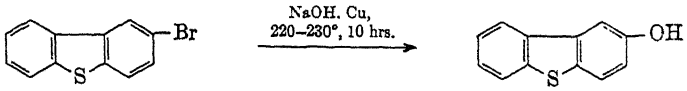
TABLES IV-6 (*continued*)

Substituent	M.p., °C.	Derivative	M.p., °C.
 2-$COCH_2$—CH_2N	106–107	HCl	197–198 (dec.)
 2-$CHOHCH_2CH_2N$	136	HCl	183–185 (dec.)
 2-$CH(OCOCH_3)CH_2CH_2N$	—	HCl	193–196 (dec.)
 4-$COCH_2CH_2N$	112	HCl	229–232 (dec.)
 4-$CHOHCH_2CH_2N$	105		
 4-$COCH_2N$	—	HCl	258–260
2-$COOCH_2CH_2N(C_2H_5)_2$	—	HCl	219
4-$COOCH_2CH_2N(C_2H_5)_2$	—	HCl	213

VII. Hydroxyl Derivatives of Dibenzothiophene

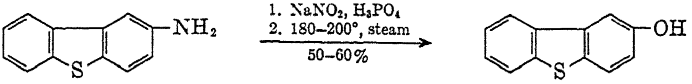
The synthesis of 1-hydroxydibenzothiophene has not been reported. It could undoubtedly be accomplished by the method used by Gilman and Jacoby (231) to obtain substituents in the 1-position. Either 1-bromo- or 1-aminodibenzothiophene should be readily convertible to 1-hydroxydibenzothiophene.

The synthesis of 2-hydroxydibenzothiophene has been accomplished by the reaction of 2-bromodibenzothiophene with both alkali and alkaline earth hydroxides (392,P-472,P-605) (eq. 72). The corresponding sulfone



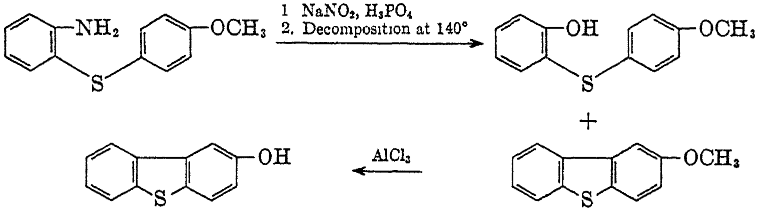
(72)

results from treatment of 2-bromodibenzothiophene 5-dioxide with alkali (P-230,P-465,127). Diazotization of 2-aminodibenzothiophene in the presence of phosphoric or hydrochloric acid followed by decomposition of the diazonium salt with superheated steam also yields 2-hydroxydibenzothiophene (392,P-465,135) (eq. 73). If superheated steam is not used, extremely low yields of the hydroxy material are obtained.



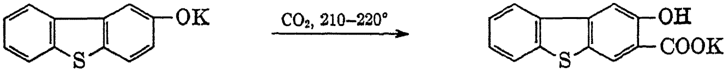
(73)

The structure of 2-hydroxydibenzothiophene has been demonstrated by means of the series of reactions shown in eq. 74 (392). The 2-hydroxydibenzothiophene formed by the previous methods gave no depression in melting point when admixed with this authentic sample.



(74)

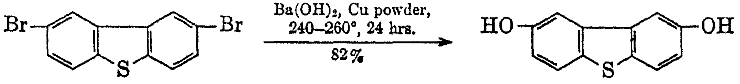
The 2-methoxydibenzothiophene formed in this reaction was reported to be a yellow oil. Further purification of this material should yield a crystalline substance. 2-Hydroxydibenzothiophene undergoes the Kolbe reaction to form the potassium salt of 2-hydroxydibenzothiophene-3-carboxylic acid (392,P-232,P-466) (eq. 75). The hydroxy sulfoxide and sulfone



(75)

also undergo this reaction to form 3-acids. A large number of amides of 2-hydroxy-3-dibenzothiophenecarboxylic acid have been prepared and are listed in Table IV-11.

2,8-Dihydroxydibenzothiophene has been made by reacting the dibromo derivative with barium hydroxide (P-605,P-708) (eq. 76). When



(76)

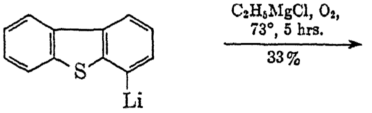
triethylene glycol was used as a solvent in this reaction, only reductive debromination took place and dibenzothiophene was the only material isolated (660).

2-Hydroxydibenzothiophene and 2,8-dihydroxydibenzothiophene have been alkylated with *tert*-amyl alcohol in the presence of zinc chloride. These alkylated products are soluble in mineral oil and act as antioxidants.

2,8-Dihydroxydibenzothiophene 5-dioxide has been made in low yields by the action of moist sodium hydroxide on 2,8-disulfodibenzothiophene 5-dioxide (127). When the corresponding dihalides were treated with caustic, they were broken down completely into biphenyl derivatives.

No synthesis for 3-hydroxydibenzothiophene has been reported, but again this material should be obtainable from the known 3-aminodibenzothiophene. This procedure has been used to prepare 3-hydroxydibenzothiophene 5-oxide (392,P-230,P-468). The oxide should also be readily convertible to 3-hydroxydibenzothiophene by reductive methods discussed previously.

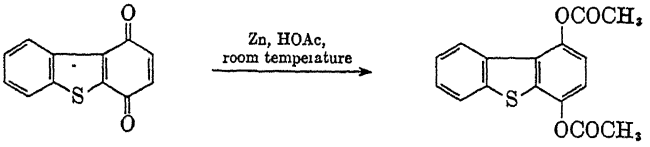
4-Hydroxydibenzothiophene has been made by reacting 4-dibenzothienyllithium with oxygen in the presence of either ethylmagnesium chloride or *n*-butylmagnesium bromide (231,649) (eq. 77). Conversion to the 4-methoxy derivative with dimethyl sulfate can be effected in 94% yield.



(77)

Chlorination of 4-hydroxydibenzothiophene with sulfuryl chloride yields a monochloro compound which is probably 1-chloro-4-hydroxydibenzothiophene (649,739).

Several di- and polyhydroxydibenzothiophenes and their derivatives have been prepared and characterized. 1,4-Diacetoxydibenzothiophene has been made by reacting 1,4-dibenzothiophene quinone with acetic acid in the presence of zinc dust (294) (eq. 78). Oxidation of this material with

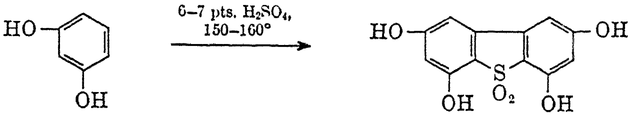


(78)

30% hydrogen peroxide in acetic acid is reported to yield 1,4-diacetoxydibenzothiophene 5-oxide.

The syntheses of 2,8-dihydroxydibenzothiophene and some of its derivatives have been discussed with the 2-hydroxydibenzothiophenes.

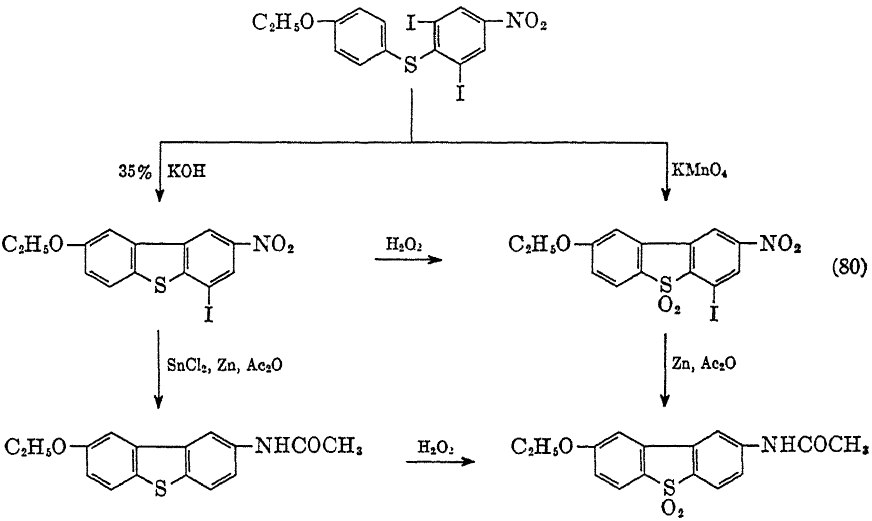
The reaction of resorcinol with sulfuric acid is claimed to yield 2,4,6,8-tetrahydroxydibenzothiophene 5-dioxide (634) (see eq. 79). A material



(79)

analyzing for 2,3,7,8-tetramethoxydinitrodibenzothiophene 5-dioxide has been obtained by the nitration of 2,3,7,8-tetramethoxythianthrene (219).

A number of substituted ethoxydibenzothiophenes and their sulfones have been made by reacting triiodonitrobenzene or triiodoaminobenzene with *p*-ethoxythiophenol to form sulfides, which can then be cyclized with potassium hydroxide or potassium permanganate (654). Equations 80 are illustrative of the method.



(80)

(I)

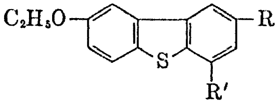
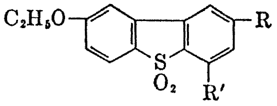
2-Acetamido-8-ethoxydibenzothiophene 5-dioxide (I) has also been synthesized from *p*-ethoxythiophenol and 3,4,5-triiodoacetamidobenzene by a series of reactions similar to those shown in eq. 80.

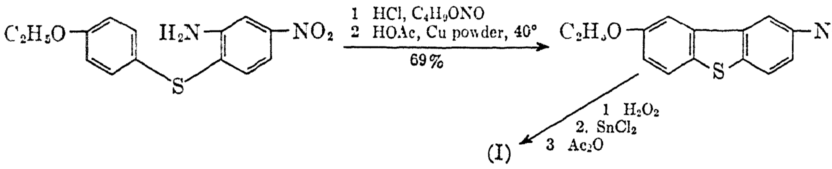
The structure of I, and therefore the structures of the intermediate compounds, was established by an independent synthesis (eq. 81). This method is an application of the Pschorr synthesis and is similar to the procedure used to establish the structures of 2-nitrodibenzothiophene (135) and 2-methoxydibenzothiophene (392). The melting points of materials made by this method appear in Table IV-8.

TABLE IV-7. Melting Points of Hydroxydibenzothiophenes and Their Derivatives

Substituent	M.p., °C.	Ref.	Deriv.	M.p., °C.	Ref.
1,4-Di-OH	—	—	Diacetoxy	126	294
			Diacetoxy-5-oxide	185	294
2-OH	156	P-472,P-465	Acetoxy	114	392
		392,P-230	5-Dioxide	264	392,P-230
	159	135,P-605			P-465,P-472
				256–258	127
			Acetoxy-5-dioxide	210	392
				269	127
			Benzoxy-5-dioxide	176	127
2,8-Di-OH	278–279	P-605	5-Dioxide	331	127
			Dibenzoxy-5-dioxide	227–228	127
2,3,7,8-Tetra-OH	—	—	Tetramethoxy-di-NO_2-5-dioxide	238	219
2,4,6,8-Tetra-OH	—	—	5-Dioxide	300	634
			Tetraacetoxy-5-dioxide	256	634
3-OH	—	—	5-Oxide	147	P-465,392
					P-230
4-OH	167	231,649	Methoxy	123	231,240,242
			Methoxy-5-dioxide	191–192	242
4-OH-1-Cl	195–196	649,739			
4-OH-1-NO_2	—	—	Methoxy	161–162	240
4-OH-di-NO_2	204	231	—		
2-$CHOHCH_3$	76–77	73	—		
	61–62	188			

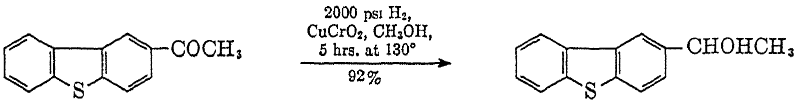
TABLE IV-8. Substituted Ethoxy Dibenzothiophenes (654)

Substituents	 M.p., °C	 M.p., °C.
R = NO_2, R′ = H	209.5–210 5	—
R = NH_2, R′ = H	109–110	—
R = $NHCOCH_3$, R′ = H	195.5–196 5	313
R = NO_2, R′ = I	222	300
R = NH_2, R′ = I	148.5–149.5	—
R = $NHCOCH_3$, R′ = I	214.5–215.5	289



(81)

The only reported dibenzothiophene having a hydroxyl group in the side chain is 2-(1′-hydroxyethyl)dibenzothiophene (73,188). This material has been made by the reduction of 2-acetyldibenzothiophene with aluminum isopropoxide in 68% yield and in even higher yields by hydrogenation in the presence of copper chromite catalyst (eq. 82). It is significant to



(82)

note that there is a fairly wide difference in the melting points reported for this material. Since Burger and Bryant (72) have definitely established that acylation yields some 4-acetyldibenzothiophene along with larger amounts of the 2-isomer, it is possible that some of the reduced 4-acetyl derivative is present as an impurity, causing a substantial lowering of the melting point.

VIII. Carbonyl Derivatives of Dibenzothiophene

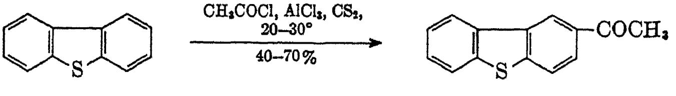
A. Aldehydes

The preparation of dibenzothiophenealdehydes or their derivatives has not been reported in the literature. The variously substituted aldehydes could probably be synthesized from the corresponding acid chlorides by the Rosenmund reduction.

B. Ketones

1. Carbonyl in Side Chain

The acylation of dibenzothiophene yields predominantly 2-acetyldibenzothiophene (231,242) (eq. 83). Burger *et al.* (71,72), in attempting to



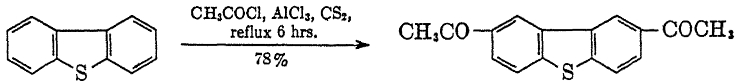
(83)

repeat the above work, obtained a 70% yield of crude acetyldibenzothiophene but only a 25% yield of pure 2-acetyldibenzothiophene. In addition, they isolated a small amount of 4-acetyldibenzothiophene. Its structure was confirmed by oxidation to the known 4-dibenzothiophenecarboxylic acid and conversion of the acid to the known methyl ester. This is the only recorded electrophilic substitutuion of dibenzothiophene at the 4-position, and it suggests that the wide differences in melting points reported for a number of materials may be due to the ineffectual removal of undiscovered isomers.

Bromination of both 2- and 4-acetyldibenzothiophene in the presence of sunlight leads to side-chain substitution (72). Attempts to brominate the nucleus in the presence of catalysts such as iron powder have not been reported.

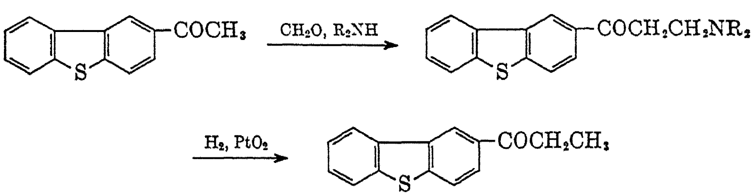
Studies of analgesic activity carried out on 2-acetyldibenzothiophene show that it exhibits depressant activity when administered to cats, but is less effective than either 3-acetylphenanthrene or 2-acetyldibenzofuran (73).

2,8-Diacetyldibenzothiophene has been prepared by a number of investigators in good yields from acetyl chloride and dibenzothiophene (242,71, 139) (eq. 84). The positions of the groups were established by converting the ketone to the known 2,8-diaminodibenzothiophene by means of the Beckmann rearrangement (see eq. 58).



(84)

2-Propionyldibenzothiophene has not been prepared by direct acylation. However, it has been isolated as a by-product from the hydrogenation mixtures of Mannich bases of 2-acetyldibenzothiophene (73) (eq. 85). Careful purification of the Mannich base before reduction resulted in an increased yield of alcohol and a suppression of the slower hydramine fission.



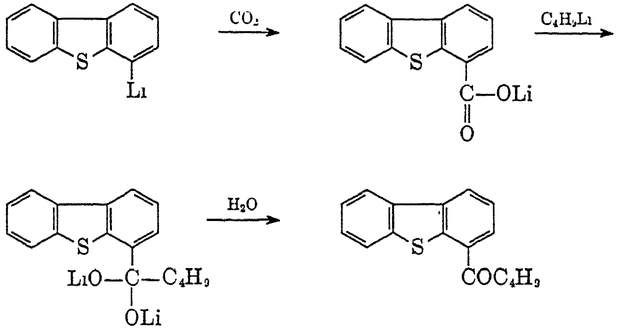
(85)

A number of other 2-acyldibenzothiophenes have been prepared by direct acylation using typical Friedel-Crafts catalysts (87,83,421,P-175).

TABLE IV-9. Physical Constants of Acyldibenzothiophenes and Their Derivatives

Substituents	M.p., °C.	Deriv.	M.p., °C.	Ref.
2-CH_3CO	111–112	Oxime	161–162	71,305,212,231
		Semicarbazone	234–235	
	B.p. 183–185 (1.0 mm.)	—	—	242
2-C_2H_5CO	72–72.5	Semicarbazone	196–198	73
2-*n*-$C_6H_{13}CO$	65	—	—	87
	B.p. 205–210 (0.05 mm.)			
2-*n*-$C_7H_{15}CO$	78	—	—	87
	B.p. 225–228 (0.08 mm.)			
2-*n*-$C_9H_{19}CO$	49	—	—	87
	B.p. 235–237 (0.07 mm.)			
2-*n*-$C_{13}H_{27}CO$	63	—	—	87
	B.p. 258–262 (0.05 mm.)			
2-*n*-$C_{17}H_{35}CO$	69–70	—	—	421
2-$C_6H_5CH_2CO$	100	Oxime	149	83
		Semicarbazone	205–206	
2-$BrCH_2CO$	115–116	—	—	72
2,8-Di-CH_3CO	208–209	Dioxime	272–274	71
	210	—	—	139
	206–208	Dioxime	266–267	242
4-CH_3CO	129–130	Semicarbazone	302–304	71,72
4-*n*-C_4H_9CO	270–271	2,4-Dinitrophenylhydrazone	270–271	651
4-$BrCH_2CO$	149–151	—	—	72
4-NH_2CH_2CO	161–162	—	—	241

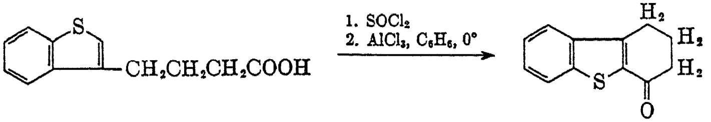
4-Valeryldibenzothiophene has been isolated in yields as high as 4.7% as a by-product in the preparation of 4-dibenzothiophenecarboxylic acid (651). The acid was prepared by metalating dibenzothiophene with butyllithium followed by carbonation. The isolation of an unsymmetrical ketone was unexpected, since in similar preparations of 4-dibenzofurancarboxylic acid only symmetrical ketones were isolated (659,658). The steps of eq. 86 account for the ketone formation. It is possible that in the case of dibenzothiophene, the greater steric effect of sulfur prevents the formation of the symmetrical ketone. An authentic sample of 4-valeryldibenzothiophene was prepared in low yields from 4-dibenzothienyllithium and valeric anhydride.



(86)

2. Carbonyl in Ring

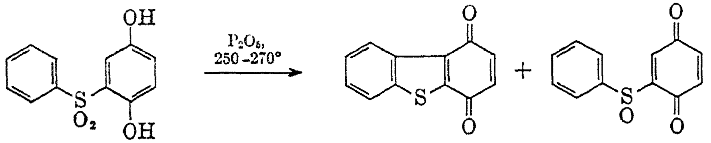
4-Oxo-1,2,3,4-tetrahydrodibenzothiophene has been made from 4-(3′-thianaphthenyl)butyric acid (77) (eq. 87). This material condenses with 1-naphthaldehyde to form 3-(1′-naphthylidene)-4-oxo-1,2,3,4-tetrahydrodibenzothiophene; m.p., 162°; picrate, m.p. 127° (90).



(87)

b.p. 212–215° (3 mm.)
m.p. 100°
Semicarbazone, m.p. 263° (dec.)
Oxime, m.p. 170°

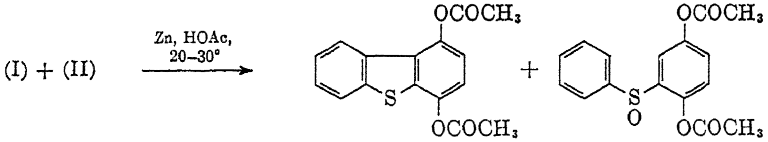
The preparation of 1,4-dibenzothiophenequinone (I) has been reported (see eq. 88) (294). The reaction of 1,4-dihydroxydiphenyl sulfone with



(I) (II)
m.p. 80–85°

(88)

phosphorus pentoxide at elevated temperatures yielded a mixture of I and II, I comprising about 10% of the mixture. I and II were not easily separable but could be converted to their acetoxy derivatives, III and IV, which were separable (eq. 89). III is quite soluble in methanol, while IV is not.



(III) (IV)

(89)

IX. Dibenzothiophenecarboxylic Acids

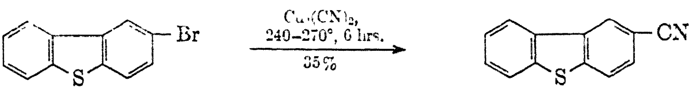
1. *Nuclear Carboxyl Group*

The carboxylic acids of dibenzothiophene form the only monosubstituted series in which all four isomers have been prepared and characterized. Their preparations are interesting since they illustrate the various methods available for obtaining particular isomers. Variations of these methods can, in many cases, be applied to the syntheses of other monosubstituted derivatives.

1-Dibenzothiophenecarboxylic acid has been obtained by the carbonation of 1-dibenzothienylmagnesium bromide (232). The synthesis of 1-bromodibenzothiophene has been discussed previously. The acid can be decarboxylated in the usual manner with copper powder in the presence of quinoline.

2-Dibenzothiophenecarboxylic acid was first prepared from 2-bromodibenzothiophene via the Grignard reaction (119). The oxidation of 2-acetyldibenzothiophene with a mixture of iodine and potassium iodide in sodium hydroxide (231) and the hydrolysis of 2-cyanodibenzothiophene (74) also yield 2-dibenzothiophenecarboxylic acid.

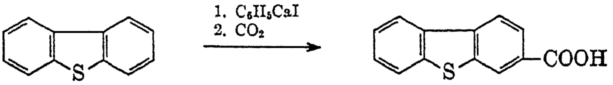
2-Cyanodibenzothiophene has been synthesized from 2-aminodibenzothiophene (74) and by reacting cuprous cyanide with 2-bromodibenzothiophene (72) (eq. 90).



(90)

2,8-Dibenzothiophenedicarboxylic acid has been made by the Grignard reaction from 2,8-dibromodibenzothiophene (119) and by the calcium hypochlorite oxidation of 2,8-diacetyldibenzothiophene (139). The melting points reported for this material varied considerably, indicating the possible presence of other isomeric acids.

The synthesis of 3-dibenzothiophenecarboxylic acid involves a rather strange and unexplained reaction (232). The metalation of condensed heterocycles such as dibenzothiophene, dibenzofuran, and *N*-ethylcarbazole always occurs at the carbon atom adjacent to the heterocyclic atom. However, in the one case, where phenylcalcium iodide is used as a metalating agent and dibenzothiophene is the heterocycle, metalation occurs at the 3-position (eq. 91). Carbonation of this metallic derivative affords the 3-acid. The metalation of dibenzofuran with phenylcalcium iodide involves the normal 4-position. There is, at present, no satisfactory explanation to account for this anomalous behavior of phenylcalcium iodide. Additional work on this reaction is under way (662).

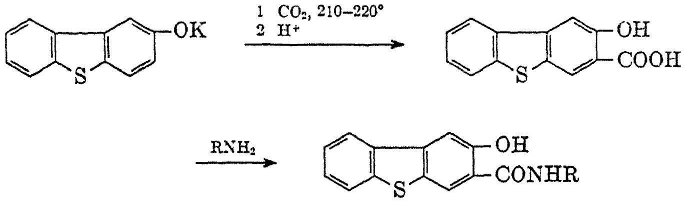


(91)

Although it is probable that the 3-acid was obtained, unequivocal proof of its structure was not presented. The data other than analyses supporting this structure were: (*1*) the acid could be decarboxylated to dibenzothiophene; (*2*) the melting points of the acid and its methyl ester were widely different from those of any of the other monosubstituted acids and methyl esters.

The metalation of dibenzothiophene to produce 3-derivatives is of little preparative value, since the yields are very poor. Since both 3-amino- and 3-bromodibenzothiophene can be synthesized by various methods, they should be suitable starting materials for the synthesis of the 3-acid.

3-Substituted acids have been prepared from 2-hydroxydibenzothiophene, its oxide and dioxide by means of the Kolbe reaction (P-473,P-588, P-591,P-230,P-466,392) (eq. 92). 2-Hydroxy-3-dibenzothiophenecarboxylic acid has been reacted with a large number of amines to form amides, which are useful intermediates in the preparation of water-soluble azo dyes. The melting points of these amides are listed in Table IV-11.



(92)

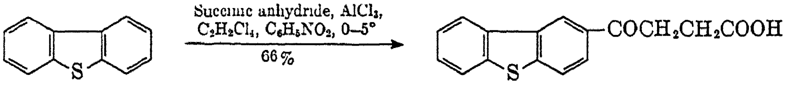
4-Dibenzothiophenecarboxylic acid has been made readily available by means of the metalation reaction. As mentioned previously, dibenzothiophene is metalated exclusively at the 4-position by all metalating agents with the exception of phenylcalcium iodide.

The best yields of acid are obtained with propyl- and butyllithium, the yields ranging from 46 to 90% of crude acid (233,235,231,237,651). With diethylcalcium and diethyl barium, the yield of 4-acid is less than 1% (238). The metalation of dibenzothiophene 5-oxide with butyllithium at −10° is also reported to yield the 4-acid (735). These metalation reactions will be discussed more thoroughly under the section on metallic derivatives of dibenzothiophene.

4-Dibenzothiophenecarboxylic acid has also been made by the oxidation of 4-acetyldibenzothiophene; the 4-acetyldibenzothiophene is obtained as a by-product of the acylation of dibenzothiophene (72).

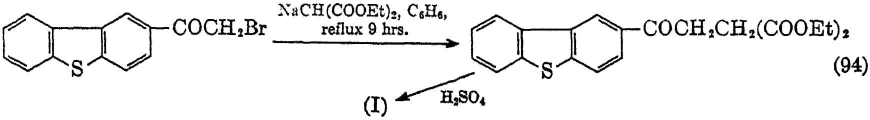
2. *Carboxyl Group in Side Chain*

The synthesis of 3-(2′-dibenzothenoyl) propionic acid (I) from dibenzothiophene and succinic anhydride has been reported by several investigators (231,526,77) (eq. 93). I has also been synthesized from ω-bromoacetyldibenzothiophene and diethyl malonate (72) (eq. 94). The reduction of I to 4-(2′-dibenzothienyl)butyric acid has been accomplished by both the Clemmensen (231,77) and the Wolff-Kishner reactions (526). 2-(2′-Carboxybenzoyl)dibenzothiophene has been prepared from phthalic anhydride

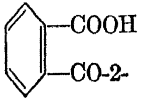


(I)

(93)

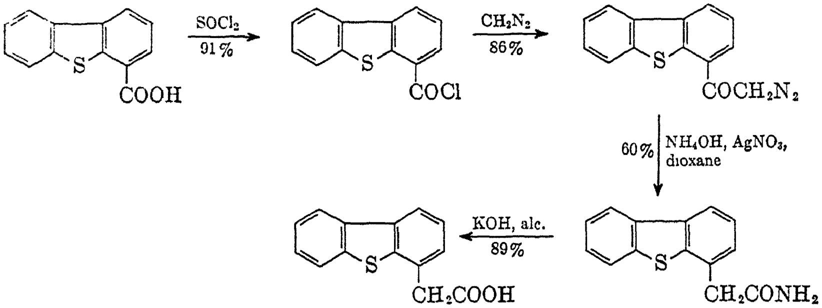


(94)

Substituent	M.p., °C.	Deriv.	M.p., °C.	Ref.
1-COOH	176–177	Me ester	72–72 5	231
2-COOH	253–255	Me ester	74–75	231,119,305
		Nitrile	159–160	72
2,8-Di-COOH	<400	—	—	139
	320	—	—	119
2-$(CH_2)_3COOH$	131	—	—	231
	129.5–130.5	—	—	526
	127	—	—	77
2-$CO(CH_2)_2COOH$	160.5–161	—	—	231
	158–159	—	—	72
	155	—	—	77
	—	Et ester	105–106	231
3-COOH	300–305 (dec.)	Me ester	129–130	232,392,P-466,P-210
3-COOH-2-OH	283	1-Carbazole amide	300	P-473,P-588
		2-(6-Methoxy)benzothiazole	270	P-473,P-588
3-COOH-2-OH-5-oxide	258	—	—	P-466,P-230
3-COOH-2-OH-5-dioxide	283–284	—	—	392,P-230
4-COOH	261–262	Me ester	94–95	72
	252–253	Me ester	95	231
		Acid chloride	159–160	241
		Amide	250–251	651,755
4-COOH-5-dioxide	337–338	Amide	236–238	651,755, 779
4-CH_2COOH	161.5–162.5	Amide	205–206	241
4,6-DiCOOH-5-dioxide	390–391	—	—	779

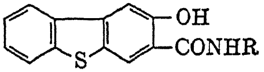
and dibenzothiophene (231). This material has been cyclized successfully to give a thianaphthenoanthraquinone. This reaction is discussed in Chapter VI.

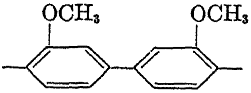
4-Dibenzothienylacetic acid has been made by the Arndt-Eistert reaction (241) (eq. 95). The 4-dibenzothienylacetic acid was prepared in connection with a program for plant hormone tests.



(95)

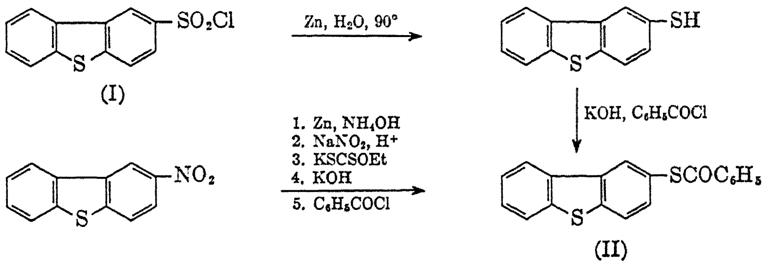
TABLE IV-11. Melting Points of Hydroxy Amides of Dibenzothiophene (P-473, P-588)



R	M.p., °C.	R	M.p., °C.
C_6H_5	289	$2\text{-}CH_3\text{-}4\text{-}ClC_6H_3$	268
$2\text{-}CH_3C_6H_4$	207	$2\text{-}CH_3\text{-}5\text{-}ClC_6H_3$	233
$4\text{-}CH_3C_6H_4$	295	$2,4\text{-}(CH_3O)_2C_6H_3$	260
$2\text{-}CH_3OC_6H_4$	195	$2,5\text{-}(CH_3O)_2C_6H_3$	203
$4\text{-}CH_3OC_6H_4$	255	$2\text{-}CH_3O\text{-}5\text{-}ClC_6H_3$	250
		$2\text{-}CH_3O\text{-}4\text{-}ClC_6H_3$	234
$2\text{-}C_2H_5OC_6H_4$	205	$3,4\text{-}Cl_2C_6H_3$	288
$4\text{-}C_2H_5OC_6H_4$	265	$2,4\text{-}(CH_3O)_2\text{-}5\text{-}ClC_6H_2$	257
$4\text{-}ClC_6H_4$	305	$2,5\text{-}(CH_3O)_2\text{-}4\text{-}ClC_6H_2$	233
$2\text{-}NO_2C_6H_4$	233	1-Naphthyl	238
$3\text{-}NO_2C_6H_4$	302		336
$2,5\text{-}(CH_3)_2C_6H_3$	190		
$2\text{-}CH_3\text{-}4\text{-}CH_3OC_6H_3$	244		
$3\text{-}CH_3\text{-}4\text{-}CH_3OC_6H_3$	245		

X. Sulfur Derivatives

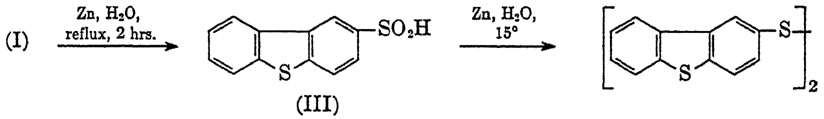
The sulfonation of dibenzothiophene yields both the 2-sulfonic and 2,8-disulfonic acids (127). The structure of 2 dibenzothiophenesulfonic acid



(96)

was established by the following series of equations (eq. 96) (126). 2-Dibenzothiophenesulfonyl chloride was reduced with zinc to the thiol and reacted with benzoyl chloride to form II. 2-Nitrodibenzothiophene could also be converted to II, proving that the original sulfonic acid was substituted at the 2-position.

I reacts with limited quantities of zinc at elevated temperatures to form 2-dibenzothiophenesulfinic acid(III) and with excess zinc at room temperature to form a disulfide (eq. 97). III reacts with thionyl chloride and dibenzothiophene to form bis(2-dibenzothienyl)sulfoxide (eq. 98).



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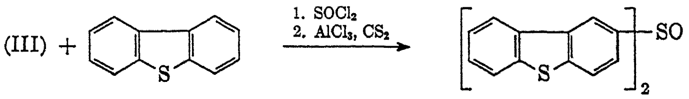
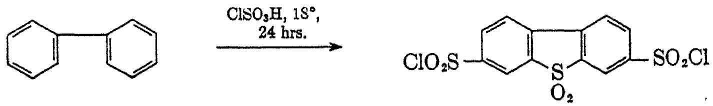


(98)

Dibenzothiophene 5-dioxide-3,7-disulfonyl chloride has been made from chlorosulfonic acid and biphenyl (409) (eq. 99).



(99)

The preparation of 3,7-dibromodibenzothiophene 5-dioxide-2,8-disulfonic acid has been reported, but the analyses listed were not correct for this material (123).

A fairly large number of sulfonic acid derivatives of benzidine sulfone have been prepared in connection with dye intermediates. These materials are discussed in the section on amines.

TABLE IV-12. Melting Points of Sulfur Derivatives of Dibenzothiophene

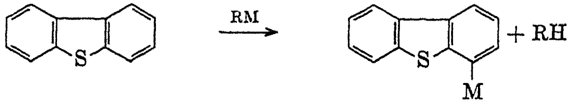
Substituent	M.p., °C.	Deriv.	M p , °C.	Ref
2-SH	81	Acetyl	122	126
		Benzoyl	116	126
$2\text{-}SC_2H_5$	93	—	—	126
$2\text{-}SO_2H$ (monohydrate)	121	—	—	126
$2\text{-}SO_3H$ (hydrate)	172	Chloride	229	126,127
$2\text{-}SO_3H$-5-dioxide (hydrate)	276	Chloride	234–235	127
2,8-Di-SO_3H-5-dioxide	—	Dichloride	337–340	127
3,6-Di-SO_3H-5-dioxide	—	Dichloride	236	409
		Dianilide	207	409
$8\text{-}SO_3H\text{-}2\text{-}NO_2$	—	Dichloride	126	257
2,2′-Disulfide	175	—	—	126
2,2′-Sulfoxide	260	—	—	126

XI. Metallic Derivatives

The preparation and study of the metallic derivatives of dibenzothiophene have been carried out almost exclusively by Gilman and his coworkers. Only 2-and 2,8-dibenzothienylmagnesium bromide had been prepared previously (119). The only other magnesium compound prepared to date, 1-dibenzothienylmagnesium bromide, was prepared by Gilman and Jacoby (231).

The mercuration of dibenzothiophene was accomplished by adding mercuric acetate to a melt of dibenzothiophene at 140–145° (231). A material melting at 215° (dec.) was obtained. The analysis indicated that the material was the monomercuriacetate contaminated with small amounts of a di- or polymercurated material. The position at which mercuration took place was not established.

Most of the metalation work on dibenzothiophene has involved metalating agents of the RM type, M being an alkali or alkaline earth metal and R an alkyl or aryl group (eq. 100). Metalation almost always involves 4-substitution; the one exception occurs with phenylcalcium iodide which metalates the 3-position (232).



(100)

Only monometalation of dibenzothiophene has been successful. The one reported attempt at dimetalation yielded, on carbonation, only dibenzothiophenecarboxylic acid (651).

Note added in proof: Gilman and Esmay (779) recently reported that dibenzothiophene 5-dioxide can be either monometalated or dimetalated. Both 4-carboxy (m.p. 337–338°) and 4,6-dicarboxydibenzothiophene 5-dioxide (m.p. 390–391°) are obtained after carbonation; the degree of substitution is controlled by the amount of *n*-butyllithium employed.

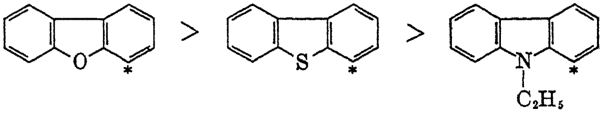
The yields of metallic derivatives, as determined by conversion to the acid, vary considerably with the nature of the R group and also with the metal. For example, the following yields of acid were obtained using an RLi metalating agent and ether as a solvent (231,651).

Metalating agent	Percent yield of 4-acid
n-Propyllithium	75
n-Butyllithium	55
Phenyllithium	12
α-Naphthyllithium	7.6
p-Anisyllithium	0
Lithium	0

The value for *p*-anisyllithium may be invalid, since, on carbonation, the acid was shown to be largely 2-methoxy-5-bromobenzoic acid. Evidently the *p*-anisyllithium preferentially metalates the unreacted *p*-bromoanisole which was used in its preparation. A number of other references also list the preparation of dibenzothienyllithium (235,240,239,242,604).

n-Amylsodium in petroleum ether affords a 37% yield of acid, while phenylsodium in benzene gives a 23% yield (233). Triphenylmethylsodium is completely ineffective as a metalating agent. Extremely low yields of the 4-acid are obtained when diethyl strontium, calcium, and barium are used as metalating agents (236,238).

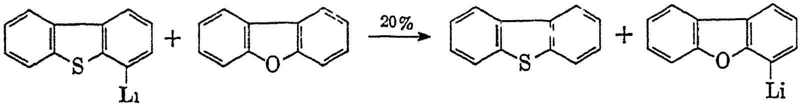
The ease of metalation of dibenzothiophene has been compared with that of dibenzofuran and *N*-ethylcarbazole and found to be as follows (234, 237):



(* denotes position at which metalation occurs)

The following procedures were used to determine the above series. Metalation of a mixture of dibenzothiophene and dibenzofuran with an amount of *n*-butyllithium sufficient to metalate one of these materials produced only 4-dibenzofurancarboxylic acid. With dibenzothiophene and *N*-ethylcarbazole, only 4-dibenzothiophenecarboxylic acid was obtained.

Also, as is shown in equations 101 and 102, dibenzofuran is metalated by dibenzothienyllithium, and dibenzothiophene is metalated by *N*-ethylcarbazoelithium. Neither of these equations can be reversed.



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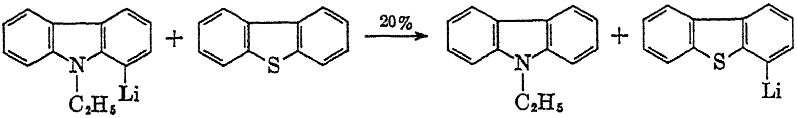
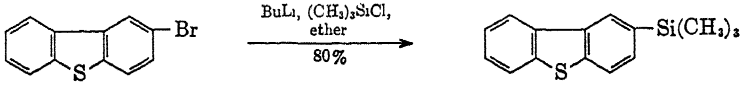


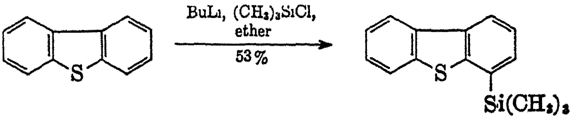
(102)

A number of silyl derivatives of dibenzothiophene have been prepared (734,657,604). 2-Trimethylsilyl- and 3-trimethylsilyldibenzothiophene have been prepared from trimethylsilyl chloride, butyllithium, and the respective bromodibenzothiophene (eq. 103). The yield of 3-trimethylsilyldibenzothiophene was 50%.



(103)

4-Trimethylsilyldibenzothiophene has been prepared from trimethylsilyl chloride, butyl lithium, and dibenzothiophene (eq. 104). 4-Triphenylsilyldibenzothiophene has been prepared in low yields (6.8%) from triphenylethoxysilane, dibenzothiophene, and butyllithium. All of these materials are easily oxidized with hydrogen peroxide to their dioxides.



(104)

The stability of the C—Si bond toward hydrogen chloride was studied and the following results were obtained:

Group	Percent cleavage of dibenzothiophene	Percent cleavage of dibenzothiophene 5-dioxide
2-$(CH_3)_3Si$	99	None
3-$(CH_3)_3Si$	97	None
4-$(CH_3)_3Si$	87	None
4-$(C_6H_5)_3Si$	None	Not run

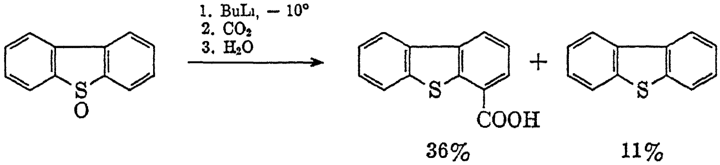
This indicates the very marked influence of the negative —SO_2— group on the stability of the C—Si linkage. The greater stability of the $(C_6H_5)_3$-Si—C bond as compared to the $(CH_3)_3$Si—C bond is not surprising and can be accounted for by resonance stabilization. This same effect has been noted in other series (663).

4-Trimethylsilyldibenzothiophene 5-dioxide has been nitrated with fuming nitric acid to form a mononitro product containing the requisite amount of silicon (604). The structure of the compound was not determined, but this reaction serves to illustrate the very stable nature of the C—Si linkage in this compound.

TABLE IV-13. Physical Constants of Silicon Derivatives of Dibenzothiophene

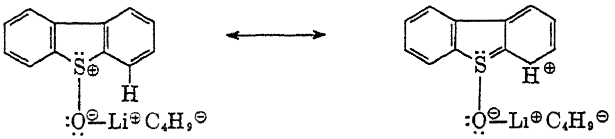
Substituent	M.p., °C.	5-Dioxide M.p., °C.	5-Dioxide Ref.
2-$Si(CH_3)_3$	48.2–49.2	164–165	657,734
3-$Si(CH_3)_3$	103.5–104.5	170.8–171.8	657,734
4-$Si(CH_3)_3$	B.p. 215–217 (20 mm.)	146–147	604
4-$Si(CH_3)_3$—NO_2	—	223–224	604
4-$Si(C_6H_5)_3$	193–194	212–213	604

The metalation of dibenzothiophene 5-oxide yields, after carbonation and hydrolysis, 4-dibenzothiophenecarboxylic acid and dibenzothiophene (735) (eq. 105). No starting material was recovered. When these metalations are conducted at higher temperatures, large amounts of an acidic gum and starting material along with smaller amounts of dibenzothiophene and 4-dibenzothiophenecarboxylic acid are obtained. The isolation of dibenzothiophene would seem to indicate that there was an initial reduction of the oxide to the thiophene which was then metalated. However, attempts to metalate dibenzothiophene at −10° yielded only starting material.



(105)

Gilman and Esmay (735) have postulated the following mechanism for this reaction (eq. 106). An initial coordination, as is shown in I, occurs between the lithium and oxygen atoms. The formation of this complex induces the electron shift shown in II. This facilitates the removal of the



(106)

proton in the 4-position by the carbanion portion of the butyllithium and is followed by rearrangement of the lithium cation to the ortho position.

Complexing between the oxygen and butyllithium without rearrangement of the lithium would on decomposition yield dibenzothiophene, while complexing after rearrangement would yield 4-dibenzothiophenecarboxylic acid. This would also explain why unreacted butyllithium is not present until after 2-3 equivalents of the metalating agent have been added. An expected by-product of this reaction, *n*-butanol, has not as yet been isolated For a further discussion of the metalation reaction, see Chapter I.

The mercuration of dibenzothiophene 5-dioxide yields a mercuriacetate, m.p. 310–315° (dec.) (650). This is the only successful direct metalation of the dioxide that has been reported. Other attempted metalations yielded, after carbonation, only acidic gums which could not be purified (650a). See note added in p. 279.

CHAPTER V

Naphthothiophenes and Other Thiophene Compounds Containing Two Carbocyclic Fused Rings

I. Introduction

The chemistry of the naphthothiophenes parallels in many ways the chemistry of thianaphthene. The majority of investigators in this series directed their work toward the synthesis of new thioindigo dyes and, consequently, many of the syntheses and reactions are similar to those of the hydroxythianaphthenes. In many cases, however, the emphasis was restricted solely to the synthesis of the final dye and a large number of the physical constants of the intermediates are of a dubious nature or althogether lacking. This is especially true of the patent literature. Wherever possible, an attempt has been made to point out these discrepancies.

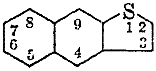
There are six possible naphthothiophene ring systems, of which five are known. The sixth, naphtho[1,2-*c*]thiophene, has not been reported in the literature. Possible methods by which this ring system could be synthesized are discussed in section VII of this chapter.

All of the naphthothiophenes, with the exception of 2-naphtho[1,8]-thiophene, are isomeric with dibenzothiophene. The 2-naphtho[1,8]-thiophene is bridged across the 1,8-positions and has an empirical formula of $C_{11}H_8S$ rather than $C_{12}H_8S$.

The discussion of the naphthothiophenes follows the order in which they appear in *Ring Index*. A table listing the physical constants of the naphthothiophene and its derivatives appears at the end of each section. Materials whose physical constants have not been reported have been omitted from these tables. Also at the end of each section is a bibliography on thioindigo dyes containing the ring system discussed in that section. The chemistry of thioindigo dyes is discussed in Chapter III.

II. Thiophanthrene Ring Systems

A. Thiophanthrene



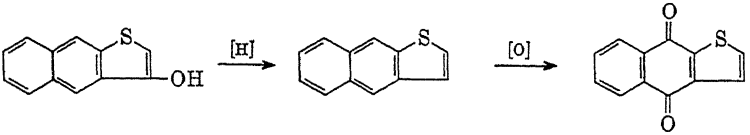
(*Ring Index* No. 1742)

Preferred Names	*Other Names*
Thiophanthrene	5,6-Benzothionaphthene
Naphtho[2,3-*b*]thiophene	β,β-Naphthothiophene

The trivial name *thiophanthrene* has been and is still widely accepted. This name was first assigned by Scholl and Seer (422). They never synthesized this material, but this ring system was part of a larger ring system that they had synthesized in their work on dyes. In order to simplify the naming of the large ring system, they arbitrarily assigned the name *thiophanthrene* to this then hypothetical naphthothiophene.

Actually, the name naphtho[2,3-*b*]thiophene is more systematic and on that basis should be preferred. However, since *Chemical Abstracts* still uses the name *thiophanthrene*, and since a number of other, larger ring systems incorporate the term *thiophanthrene* in their nomenclature, it was decided to use this name throughout this and subsequent sections.

Thiophanthrene has been prepared by the reduction of 3-hydroxythiophanthrene (378) (eq. 1). The procedure used to carry out this reduction was not reported. Oxidation of thiophanthrene with chromic acid yielded the known 4,9-thiophanthraquinone. All attempts to prepare thiophanthrene by the reduction of 4,9-thiophanthraquinone were unsuccessful (467).

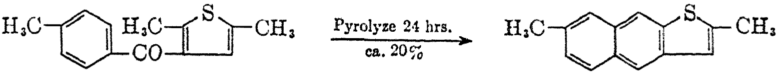


(1)

No reactions of thiophanthrene have been reported. It is probably quite similar to thianaphthene in chemical reactivity and would probably undergo most of the reactions of thianaphthene.

B. Alkyl and Aryl Derivatives of Thiophanthrene

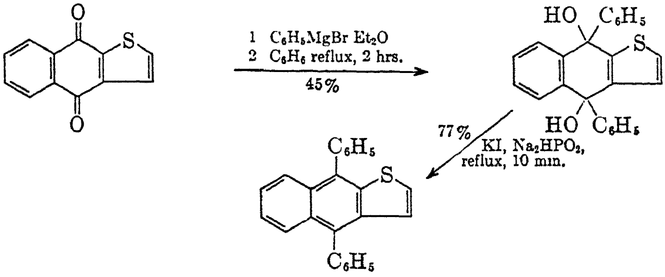
The only alkylthiophanthrenes reported in the literature have been made by means of the Elbs reaction (81) (eq. 2). As is shown in eq. 2,



(2)

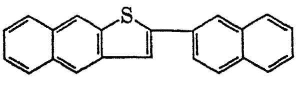
2,7-dimethylthiophanthrene is obtained by the cyclodehydration of 3-(4′-toluyl)-2,5-dimethylthiophene. 2-Methyl- and 2-methyl-7-ethylthiophanthrene have also been made by this method.

4,9-Diphenylthiophanthrene has been made from 4,9-thiophanthraquinone and phenylmagnesium bromide (179) (eq. 3).

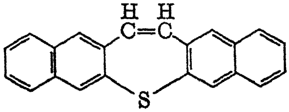


(3)

From the reaction of 2-methylnaphthalene and sulfur, Friedman (667) isolated a material that analyzed as $C_{22}H_{14}S$ and he assigned to it structure IB:

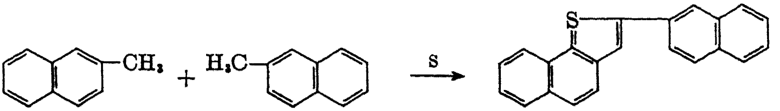


(IA)



(IB)

Horton (300) studied the reaction of tolune and sulfur and showed that 2-phenylthianaphthene was formed. He concluded that if the same free radical mechanism developed for the reaction of sulfur and toluene also applied to the reaction of sulfur and 2-methylnaphthalene, then the product isolated by Friedman should be 2-(2′-naphthyl)thiophanthrene (IA) rather than IB. A compound equally as probable as IA, 2-(2′-naphthyl) naphtho[1,2-*b*] thiophene could form if condensation occurred at carbon-1 rather than carbon-3 (eq. 4). Horton could also satisfactorily account for

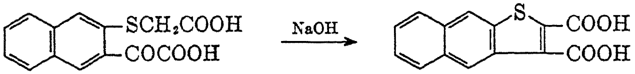


(4)

the formation of compounds containing two sulfur atoms which could not be accounted for on the basis of structure IB (see Chapter VII, part e).

C. Acids of Thiophanthrene

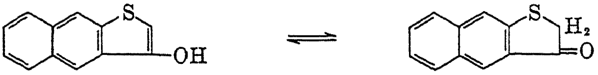
2,3-Thiophanthrenedicarboxylic acid has been made as shown in eq. 5 (378). This is the same method used for the preparation of 2,3-thianaphthenedicarboxylic acid (46). 2,3-Thiophanthrenedicarboxylic acid was successfully dehydrated to the anhydride but attempts to condense it with benzene were unsuccessful.



(5)

D. 3-Hydroxythiophanthrene and Derivatives

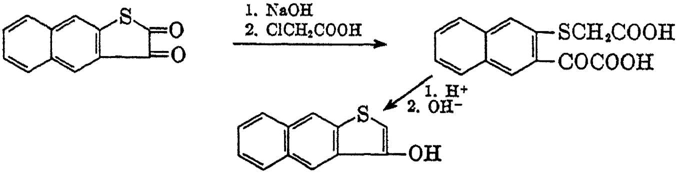
3-Hydroxythiophanthrene is quite similar to 3-hydroxythianaphthene. It also exists in both keto and enol forms (eq. 6). The ability of the hydroxy form to exist in its tautomeric keto state is a prime prerequisite of thioindigo intermediates. Although it is a debatable point as to which tautomer represents more nearly the correct form, it was decided, in the interest of simplification, to write and list all derivatives in the hydroxy form. This rather arbitrary designation has been used throughout Chapter I and subsequent sections.



(6)

2,3-Dihydro-3-oxothiophanthrene
2,3-Naphthothioindoxyl

3-Hydroxythiophanthrene (II) has been synthesized from 2,3-thiophanthraquinone (P-38,160). As was demonstrated previously, if treatment with acid is omitted, decarbonylation does not take place and

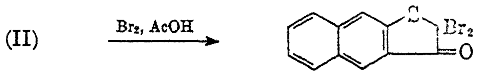


(II)

(7)

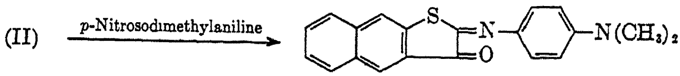
cyclization to the 2,3-diacid occurs. It is also necessary to have the carboxyl group in the 3-position, since the cyclization of 2-naphthylthioglycolic acid yields 1-hydroxynaphtho[2,1-*b*]thiophene (P-217).

The only substitution reactions reported for II involve the keto form. The bromination of II yields the 2,2-dibromo derivative (P-506,P-405) (eq. 8).



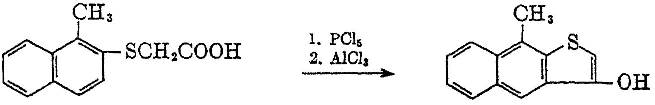
(8)

Refluxing of the dibromo material with 40% acetic acid converts it to the 2,3-thiophanthraquinone. II can also be coupled with nitroso compounds to form anils which are suitable intermediates for the preparation of mixed naphthindigo dyes (P-405,P-506) (eq. 9).



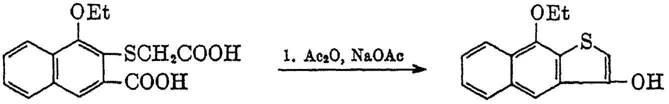
(9)

The only monosubstituted 3-hydroxythiophanthrenes that have been reported are substituted in the 9-position. These result from the cyclization of 1-substituted 2-naphthylthioglycolic acids. For example, 9-methyl-3-hydroxythiophanthrene has been prepared as shown in eq. 10 (P-630, P-424). Other 9-substituted derivatives made by this method are the chloro and bromo derivatives (298,414,P-395,P-503,P-228,P-403,P-44).



(10)

9-Ethoxy-3-hydroxythiophanthrene has been made as illustrated in eq. 11 (P-425).



(11)

The preparation of 9-carboxythiophanthrene from 1,3-dicarboxy-2-naphthylthioglycolic acid has also been reported (P-460,P-222). This is surprising, since in most cases, when the 1-position is occupied by a carboxyl group, ring closure occurs at that position to form a naphtho[2,1-*b*]-thiophene.

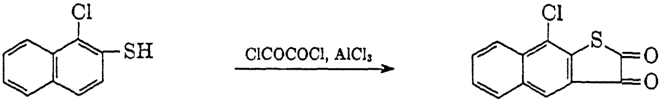
Although no monosubstituted derivatives of 3-hydroxythiophanthrene other than those substituted in the 9-position have been reported, others could probably be prepared from substituted 3-carboxy-2-naphthylthioglycolic acids.

Several dihalogenated-3-hydroxythiophanthrenes have been prepared by methods employing the above ring closures (298).

E. 2,3-Thiophanthraquinone and Derivatives

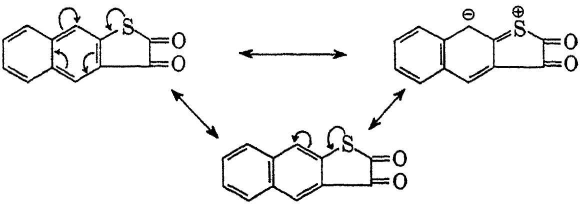
2,3-Thiophanthraquinone has been made by the acid hydrolysis of anils of 3-hydroxythiophanthrene (P-506,P-39,378) and by refluxing 2,2-dibromo-3-oxo-2,3-dihydrothiophanthrene with 40% acetic acid (P-506).

Substituted 2,3-thiophanthraquinones have been made by the condensation of oxalyl chloride with 1-substituted-2-mercaptonaphthalenes (P-611,P-35,P-222) (eq. 12). The 9-chloro, bromo, and carboxy derivatives have been prepared and characterized. As was the case with substituted 3-hydroxythiophanthrenes, only the 9-derivatives have been reported.



(12)

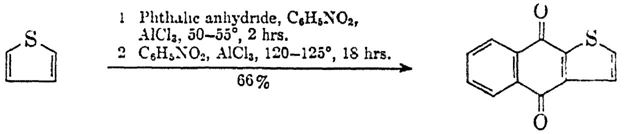
The bromination of 2,3-thiophanthraquinone leads to a monobromo derivative (P-56). No attempt was made to determine its structure. However, the monobromo derivative does have the same melting point as the 9-bromo-2,3-thiophanthraquinone made by the ring closure of 1-bromo-2-mercaptonaphthalene with oxalyl chloride (P-35,P-611). Also on the basis of possible resonating structures, it seems plausible that initial substitution should occur at the 9-position (eq. 13).



(13)

F. 4,9-Thiophanthraquinone and Derivatives

4,9-Thiophanthraquinone, commonly called thiophanthraquinone, is best prepared by reacting thiophene and phthalic anhydride in the presence of aluminum chloride at elevated temperatures (P-665,752) (eq. 14). This

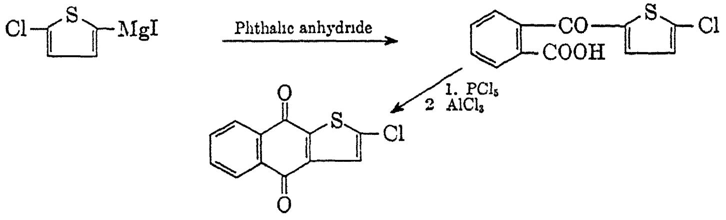

1 Phthalic anhydride, C₆H₅NO₂, AlCl₃, 50–55°, 2 hrs.
2 C₆H₅NO₂, AlCl₃, 120–125°, 18 hrs.
66%
S
O
O
S

(14)

reaction can be carried out in a one-stage process without the isolation of the intermediate 2-(2′-thenoyl)benzoic acid. When this reaction is carried out at temperatures below 30°, polymerization of the thiophene by the aluminum chloride becomes the predominant reaction. As pointed out by Weinmayr, it is rather surprising that at elevated temperatures polymerization of the thiophene does not occur.

4,9-Thiophanthraquinone has also been made by the cyclization of 2-(2′-thenoyl)benzoic acid with both phosphorus pentoxide and sulfuric acid (179,467) and by ring closure of 2-(2′-thenoyl)benzoyl chloride with aluminum chloride (668).

A number of 2- and 3-substituted thiophanthraquinones have been prepared by reacting phthalic anhydride with substituted thiophenes in the presence of aluminum chloride (P-668,P-668a,P-663,P-664,752). 2-Methyl-, 3-methyl-, and 2-chlorothiophanthraquinones have been prepared by this method. 2-Chlorothiophanthraquinone has also been prepared from phthalic anhydride and 5-chloro-2-thienylmagnesium iodide (668) (eq. 15).

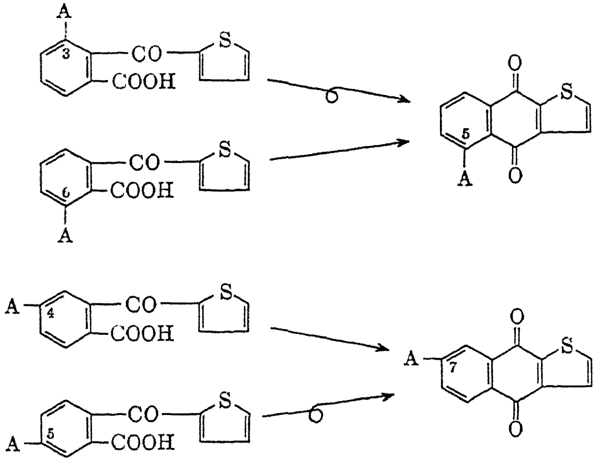


(15)

A large number of thiophanthraquinone derivatives have been prepared by the cyclization of benzene-substituted *o*-thenoylbenzoic acids (753,P-703, P-702).* A variety of rearrangements, which are dependent on the nature of the substituents, occur during these ring closures. Thus, when a nitro or chloro group is meta to the thenoyl grouping, normal cyclization occurs, but when these groups are in either the ortho or para positions, rearrangement takes place (eq. 16).

---

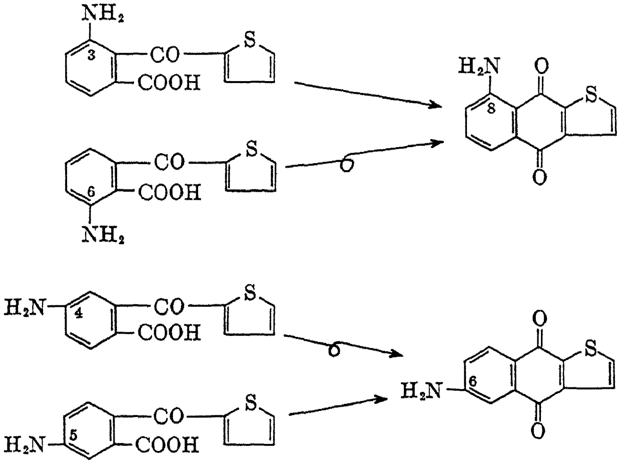
* A number of the thiophanthrene derivatives listed in these references had been previously assigned incorrect structures (P-680,P-671,P-670,P-679). These structures have now been corrected (753,P-703,P-702). References in the text and Table V-1 include only those articles and patents which contain the corrected structures.



(16)

Note added in proof: Two other nitrothiophanthraquinones, presumably the 5- and 7-nitro isomers, have been synthesized recently (781).

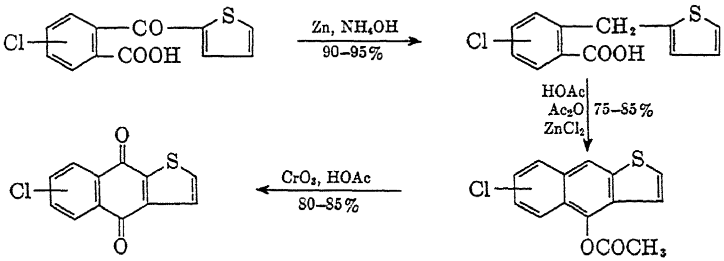
In the case of the aminothenoylbenzoic acids, rearrangement occurs when the amino groups are meta to the thenoyl group, and normal ring closure takes place when these groups are in the ortho and para positions (eq. 17).



(17)

The above ring closures were effected with 96% sulfuric acid by heating the reaction mixture to 135–145° for one to five minutes and quenching with water. In the cyclization of the amines, a boric acid-sulfuric acid mixture was used. These rearrangements are independent of the condensing agent; *e.g.*, sulfuric acid, hydrogen fluoride, and aluminum chloride yielded the same isomers.

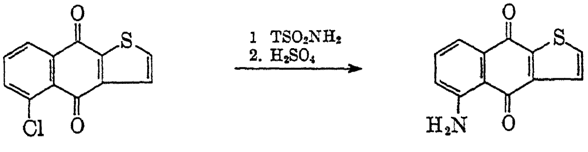
The structures of these substituted thiophanthraquinones were established by independent syntheses (753). The four possible benzene-substituted monochlorothiophanthraquinones were prepared as shown in eq. 18.



(18)

The 5-chloro derivative was identical with the material obtained from the cyclization of either the 3- or 6-chloro-2-(2-thenoyl) benzoic acids, while the 7-chloro derivative was identical with the product from the cyclization of the 4- and 5-chloro-2-(2-thenoyl)benzoic acids.

Authentic samples of 5- and 8-aminothiophanthraquinones were prepared by amination with *p*-toluenesulfonamide followed by hydrolysis (eq.

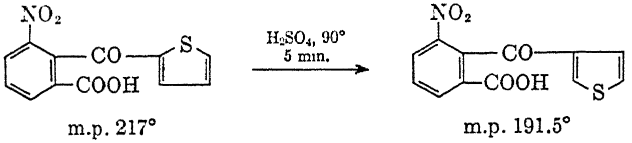


(19)

19). These amino derivatives could be converted back to the chloro derivatives via the Sandmeyer reaction.

Attempts to synthesize the β- (6 and 7) aminothiophanthraquinones by direct amination were unsuccessful. The structures of the β-aminothiophanthraquinones obtained from the ring closure of the 4- and 5-amino-2-(2-thenoyl)benzoic acids and from the cyclization of the 4- and 5-nitro-(2-thenoyl)benzoic acids followed by reduction were established by converting them to the known chlorothiophanthraquinones. The results showed that the 5-amino and 4-nitro derivatives ring closed directly, while the 4-amino and 5-nitroderivatives cyclized with rearrangement.

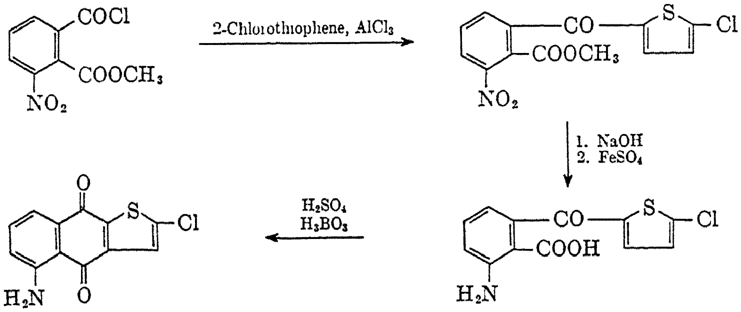
Schroeder and Weinmayr (753) were able to show that at low temperatures isomerization of the keto acids occurred (eq. 20). The structure of



(20)

the 3-nitro-2-(3-thenoyl)benzoic acid was not established, but its formation seems probable. This then presumes that the rearrangement involves a shift of the entire nitronaphthaloyl radical. Attempts to effect a similar rearrangement with the β isomers yielded only starting materials or the thiophanthraquinones.

5-Amino-2-chloro-4,9-thiophanthraquinone has been made according to equations 21 (P-606,P-607,P-675).

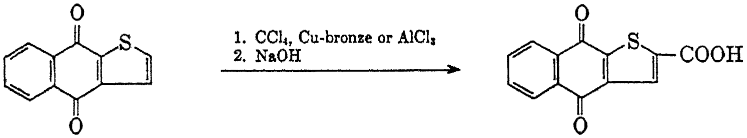


(21)

2-Bromothiophanthraquinone is formed from the bromination of 4,9-thiophanthraquinone with bromine in glacial acetic acid in a sealed tube (678). Attempts to brominate thiophanthraquinone with *N*-bromosuccinimide were unsuccessful.

The nitration of thiophanthraquinone yields a mononitro derivative which has not been identified, but which is probably 2-nitrothiophanthraquinone (678). This material can be reduced to the corresponding amino derivative.

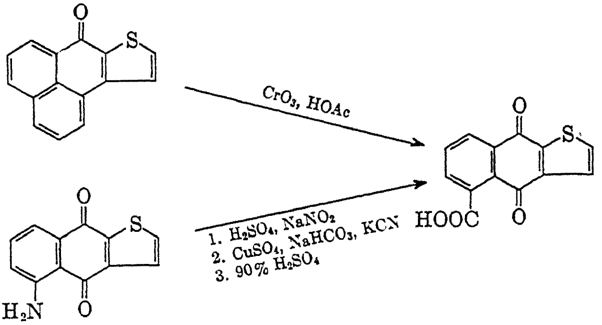
Thiophanthraquinone reacts with carbon tetrachloride to form a trichloromethyl derivative which can be hydrolyzed to the acid (P-603,752) (eq. 22). No yields were listed.



(22)

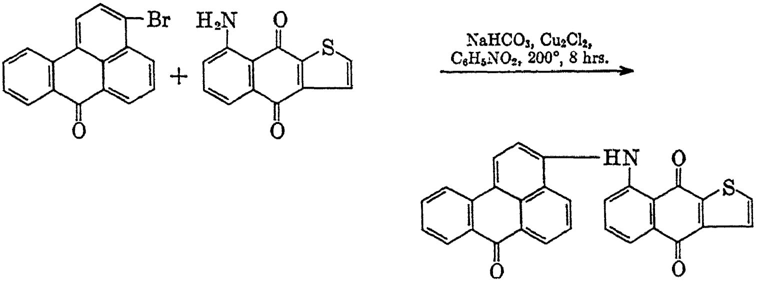
The structure of the acid was shown to be identical with the one formed from the oxidation of 2-methylthiophanthraquinone. 2,2′-Bis(4,9-thiophanthraquinonyl)ketone is a by-product of this reaction.

4,9-Thiophanthraquinone-5-carboxylic acid has been made by the oxidation of 7*H*-benzo[*ef*]thiophanthrene-7-one (4,5-benzothiophanthrone) and from 5-aminothiophanthraquinone (754) (eq. 23). The 4,9-thiophanthraquinone-8-carboxylic acid has been made by the oxidation of 7*H*-benzo[*jk*]-thiophanthrene-7-one (8,9-benzothiophanthrone) (754). The syntheses of these benzothiophanthrones are discussed in Chapter VI.

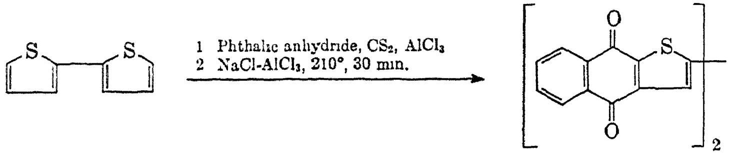


(23)

A number of thiophanthraquinone dyes have been prepared (P-696, P-701). The aminothiophanthraquinones form violet-brown dyes when coupled with materials such as 7*H*-3-bromobenz[*de*]anthracene-7-one (P-606,P-607,P-675) (eq. 24). It is claimed that these dyes, when treated with alcoholic caustic, show a very marked and unexpected depth in shade and improved light fastness over the analogous benzene derivatives. The synthesis of 2,2′-bi-4,9-thiophanthraquinone has been achieved in low yields by reacting phthalic anhydride with 2,2′-dithienyl (486) (eq. 25). This material is orange-red and forms a wine-red dye from an alkaline vat.

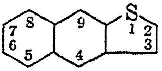


(24)


S
S
1 Phthalic anhydride, CS$_2$, AlCl$_3$
2 NaCl-AlCl$_3$, 210°, 30 min.
O
S
O
2

(25)

ABLE V-1. Melting Points of Thiophanthrene and Its Derivatives.



Substituent	M.p., °C.	Ref.
	Thiophanthrene	
None	189	378
2-CH$_3$	175	81
2,7-Di-CH$_3$	209	81
2-CH$_3$-7-C$_2$H$_5$	165	81
4,9-Di-C$_6$H$_5$	216	179
2-(2′-Naphthyl)	167	300,667
3-OH	138	P-174
3-OH-9-Cl	149–150	P-395
3-OCOCH$_3$-9-Cl	106	P-503
3-OH-9-Br	155	P-44,P-503
3-OCOCH$_3$-9-Br	104	P-44
3-OH-9-COOH	174–175	P-222,P-460
2,3-Di-COOH	264–265	378
2,3-Dianhydride	273–274	378
4,9-Di-C$_6$H$_5$-4,9-Di-OH	236	179
4-OCOCH$_3$	121–122	753
4-OCOCH$_3$-5-Cl	187–188	753
4-OCOCH$_3$-6-Cl	155–156	753
4-OCOCH$_3$-7-Cl	155	753
4-OCOCH$_3$-8-Cl	88	753
4-OCOCH$_3$-8-Cl-2(?)-CH$_3$CO	211–212	753
	2,3-Thiophanthraquinone	
None	171	493
	168	P-506
	166	378
2-p(CH$_3$)$_2$NC$_6$H$_4$N=	190–191	P-405,P-506,378
2-Di-Br	158	P-506
9-Cl	194	P-35,P-506,P-611
9-Cl-2-p(CH$_3$)$_2$NC$_6$H$_4$N=	272	P-506
9-Br	216–217	P-35,P-611,P-56
9-COOH	296–297	P-222

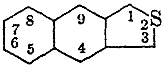
TABLE V-1 (*continued*)

Substituent	M p., °C.	Ref
4,9-Thiophanthraquinone		
None	230	P-665,752
	229	179
	227–228	378,467,678
2-CH_3	249–250	P-678,752
	247–248	678
2-C_2H_5	235–236	678
3-CH_3	179–180	P-678,752
2-Cl	178–179	P-664,678,752
5-Cl	226	753
6-Cl	214	753
7-Cl	190	753
8-Cl	172	753
5,8-Di-Cl	225–228	P-679,752
5,6,7,8-Tetrachloro	202–203	P-679,752
2-Br	180–181	678
7-Br	201–202	753
5-NH_2	237	753
	232–233	P-703
—, 5-tosyl	257	753
—, 5-(2-thenoyl)	259	753
7-NH_2	270–271	P-703
8-NH_2	231–232	753,P-703
—, 8-tosyl	221	753
—, 8-(2-thenoyl)	225	753
2-CH_3CO-8-Cl (?)	328–329	753
5-NH_2-2-Cl	222–223	P-606,P-675
2-COOH	289–290	P-603
	293–294	752
5-COOH	283–284	754
5-CN	200–215	754
8-COOH	273–274	754

References for Thioindigo Dyes Containing the Thiophanthrene Ring System

160
161
162
163
166
205
258
260
378
521
P-29
P-31
P-35
P-40
P-41
P-44
P-45
P-52
P-97
P-130
P-174
P-194
P-222
P-228
P-364
P-395
P-397
P-403
P-405
P-424
P-425
P-521
P-614
P-619

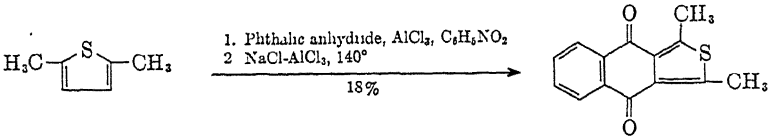
III. Naphtho[2,3-*c*]thiophene Ring Systems



(*Ring Index* No. 1742F)

Preferred Name	*Other Name*
Naphtho[2,3-*c*]thiophene	β-Thiophanthrene

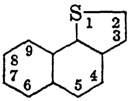
This ring system has been reported only once in the literature (484). 1,3-Dimethylnaphtho[2,3-*c*]thiophene-4,9-dione has been synthesized from phthalic anhydride and 2,5-dimethylthiophene (eq. 26). If sulfuric acid is used in the second step, a much poorer yield is obtained.

 (26)

m.p. 175–176°

IV. Naphtho[1,2-*b*]thiophene Ring Systems

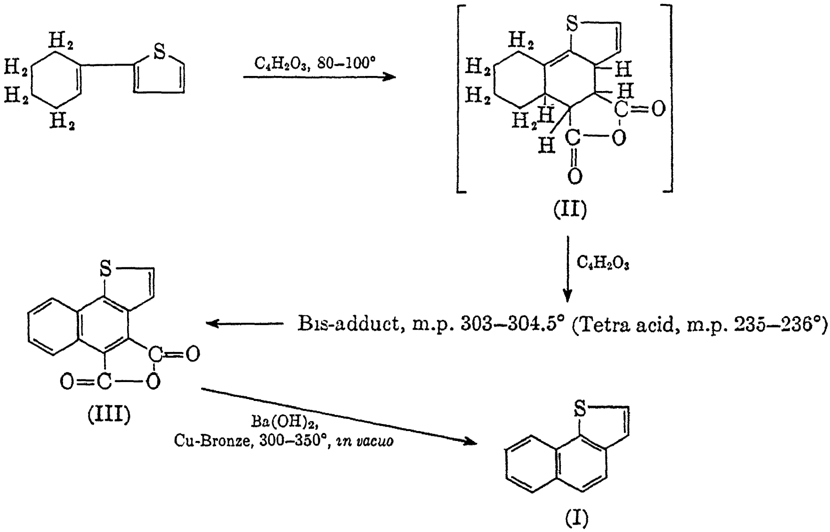
A. Naphtho[1,2-*b*]thiophene



(*Ring Index* No. 1744)

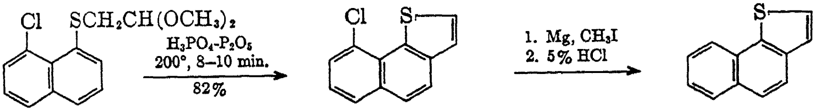
Preferred Name	*Other Names*
Naphtho[1,2-*b*]thiophene	α-Naphthothiophene 1,2-Naphthothiophene Naphtho-1′,2′:2,3-thiophene 6,7-Benzothionaphthene

The preparation of naphtho[1,2-*b*]thiophene(I) involves the initial addition of maleic anhydride to 1-(2′-thienyl)cyclohexene to form an adduct, II (537) (eq. 27). This adduct can combine with an additional mole of maleic anhydride to form a bis adduct of undetermined structure. Upon treatment with sulfur at elevated temperatures, the bis adduct loses the elements of maleic anhydride and hydrogen and forms the anhydride (III), which can be decarboxylated by customary procedures to yield I.


C₄H₂O₃, 80–100°
(II)
C₄H₂O₃
Bis-adduct, m.p. 303–304.5° (Tetra acid, m.p. 235–236°)
(III)
Ba(OH)₂,
Cu-Bronze, 300–350°, in vacuo
(I)

(27)

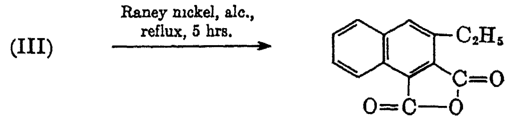
The preparation of I by the method of eq. 27A has been reported recently (765). It may be of interest to point out that if the chloro group is not in the 8-position, cyclization occurs at that point to yield a thiapyran derivative.



(27A)

I could probably be prepared by either the reduction of its 3-hydroxy derivative or by the dry distillation of its 2,3-dicarboxylic acid over lime (378).

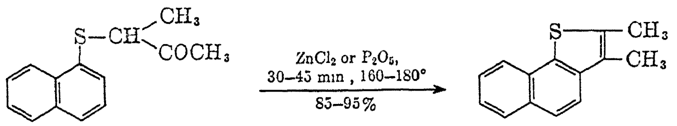
Treatment of III with Raney nickel (10:1) leads to the rupture of the thiophene ring and removal of sulfur (538) (eq. 28). The melting points of a number of methyl and dimethyl derivatives of III, which were also prepared by the Diels-Alder reaction, are listed in Table V-2.



(28)

B. Alkyl Derivatives of Naphtho[1,2-*b*]thiophene

2,3-Dimethylnaphtho[1,2-*b*]thiophene has been prepared as shown in eq. 29 (525). It is conceivable that the above ring closure could take place

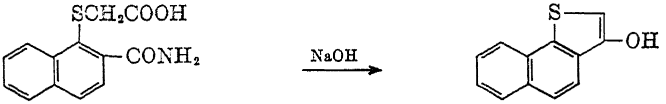


(29)

at the 8-position to form a naphthothiapyran derivative. The structure shown above was proved to be correct by reducing the compound with Raney nickel to 2-*sec*-butylnaphthalene. Ring closure at the 8-position would have yielded 1-*sec*-butylnaphthalene.

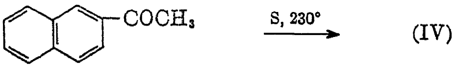
C. 3-Hydroxynaphtho[1,2-*b*]thiophene and Derivatives

3-Hydroxynaphtho[1,2-*b*]thiophene (IV) has been synthesized by a variety of methods. Most of these involve the cyclization of 1-naphthylthioglycolic acids containing a carboxyl, carbamyl, or cyano grouping in the 2-position (205,456) (eq. 30). IV has also been made by reacting sulfur with 2-acetylnaphthalene (171) (eq. 31). The mechanism of this reaction



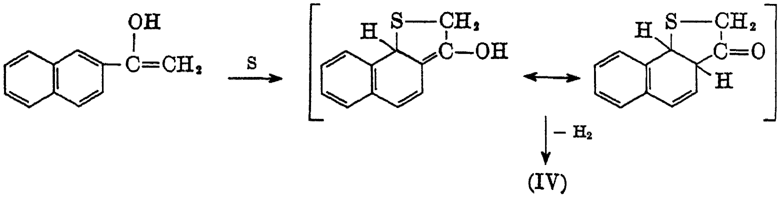
(IV)

(30)



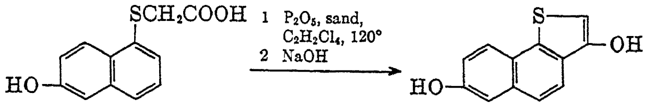
(31)

has not been studied. It seems plausible that the initial step would be a 1,4-addition of sulfur to the enol form of 2-acetylnaphthalene. The resulting material is then dehydrogenated by additional sulfur (eq. 32).



(32)

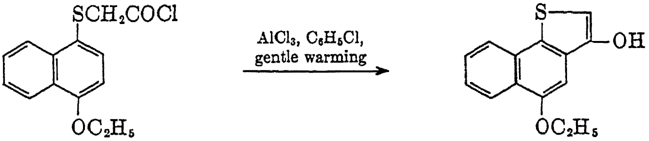
IV has also been synthesized from naphtho[1,2-*b*]thiophenequinone (P-503) by the method described for the preparation of 3-hydroxythiophanthrene (see eq. 7). 3,7-Dihydroxynaphtho[1,2-*b*]thiophene has been prepared from 2-hydroxy-5-naphthylthioglycolic acid (308) (eq. 33). It is claimed that an ester of the naphthylthioglycolic acid and the hydroxythio-



(33)

phene is formed which can then be saponified by alkali. Approximately 10% of the thioindigo dye is also formed in this reaction. The 3,8-dihydroxy derivative has also been made in the same manner.

The 5-ethoxy and 8-ethoxy derivatives of IV have been made by ring closure of substituted acid chlorides (P-528) (eq. 34). The 5-ethoxy isomer



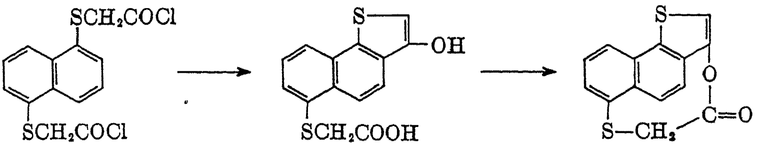
(34)

has also been made by the conventional ring closure of the thioglycolic acid (P-94).

The cyclization of 8-chloro-1-naphthylthioglycolic acid in the presence of hydrofluoric acid is reported to yield 9-chloro-3-hydroxynaphtho[1,2-*b*]-thiophene in quantitative yields (678). When sulfuric acid is used as condensing agent, some sulfonation and oxidation occur.

A number of halogenated and dihalogenated derivatives of IV have been prepared by conventional methods previously discussed (P-503,P-174, P-246,P-602,P-154).

The cyclization of 1,5-naphthyldimercaptoacetyl chloride yields 3-hydroxynaphtho[1,2-*b*]thiophene-5-thioglycolic acid (116) (eq. 35). This



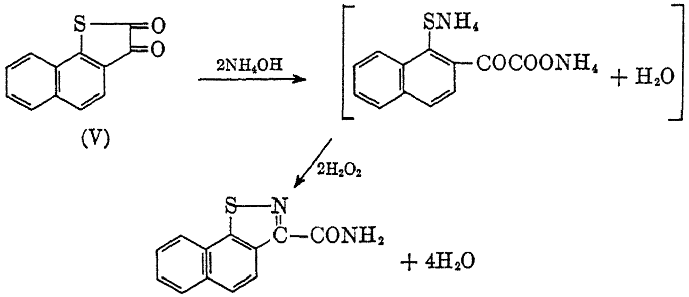
(35)

material loses water to form the lactone. The open-chain compound forms a monoacetate. Alkaline oxidation of both the open-chain material and the lactone yields the same thioindigo dye. This is a disodium salt which can be converted to the free dye with hydrochloric acid.

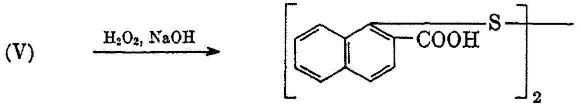
D. 2,3-Naphtho[1,2-*b*]thiophenequinone and Derivatives

2,3-Naphtho[1,2-*b*]thiophenequinone (V) has been made by refluxing the dibromo derivative or the anil of 3-hydroxy-2,3-naphtho[1,2-*b*]thiophene with acid (P-510,492).

V undergoes several interesting reactions. It reacts with caustic to form the expected 1-mercapto-2-glyoxalic acid (P-503). The reaction of V with concentrated ammonia and hydrogen peroxide yields a 1,2-thiazole ring (492). This reaction product is rather unexpected, but it can be accounted for by equations 36. With hydrogen peroxide and sodium hydroxide, the following transformation occurs (495) (eq. 37). The disulfide reduces potassium permanganate at room temperature.



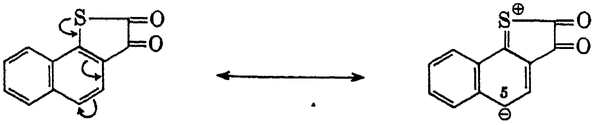
(36)



(37)

A number of quinoxalines have been prepared by reacting V with orthodiamines (155). These quinoxalines dye wool from an acid bath.

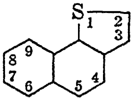
The bromination of V leads to a monobromo derivative. The structure of this material was not determined. However, on the basis of the following resonating structures, it appears probable that substitution would take place at the 5-position (eq. 38). No other bromo derivatives of V have been reported.



(38)

A number of halogenated derivatives of V have been prepared by the ring closure of halogenated-1-mercaptonaphthalenes with oxalyl chloride (P-611,P-405,P-35,P-38). The melting points of these materials are listed in Table V-2.

TABLE V-2. Melting Points of Naphtho[1,2-*b*]thiophene and Its Derivatives



Substituent	M.p., °C.	Ref.
Naphtho[1,2-*b*]thiophene		
None	B.p. 140–142 (10 mm.)	537,765
—, picrate	141–142	537,765
2,5-Di-CH_3	108.5–109	525
—, picrate	143–144	525
—, 1,1-dioxide	257–258	525
8- Cl	81–82	765
—, picrate	160	765
3-OH	142	205,P-503
3,7-Di-OH	102–105	308
3,8-Di-OH	137–139	308
3-OH-5-OC_2H_5	157–158	P-94,P-528
3-OH-6-OCH_3	173	P-212
3-OH-8-OCH_3	116–117	P-528
3-OH-5-Cl	165	P-503
3-OH-6-Cl	176	P-503
3-OH-7-Cl	153–155	P-174
3-OH-9-Br	180–181	P-246
3-OH-4,7-di-Cl	209–210	P-602
3-OH-4,8-di-Cl	190–192	P-602
3-OH-5,8-di-Cl	183–184	P-602
3-OH-6,9-di-Cl	186	P-602
	183–184	P-154
4,5-Di-COOH	—	—
(anhydride)	251	537
7-CH_3-4,5-di-COOH	—	—
(anhydride)	219	537
8-CH_3-4,5-di-COOH	—	—
(anhydride)	193	537
9-CH_3-4,5-di-COOH	—	—
(anhydride)	320	537
6,9-Di-CH_3-4,5-di-COOH	—	—
(anhydride)	293	537
2,3-Naphtho[1,2-*b*]thiophenequinone		
None	173	492
2-$C_6H_4CH=$	181	205
2-*p*$(CH_3)_2NC_6H_4N=$	205	P-506
	250	P-405

Table continued

TABLE V-2 (*continued*)

Substituent	M.p., °C.	Ref.
2,3-Naphtho[1,2-*b*]thiophenequinone (*continued*)		
5-Cl	220	P-35,P-611
5-Cl-2-di-Br	178	P-405,P-506
5-Cl-2-*p*$(CH_3)_2NC_6H_4N=$	269	P-405,P-506
6-Cl	183	P-611
9-Cl	238–239	P-35
6,9-Di-Cl	—	—
6,9-Di-Cl-2-*p*$(CH_3)_2NC_6H_4N=$	247–248	P-602
5-Br	241	P-56

References for Thioindigo Dyes Containing the Naphtho[1,2-*b*]thiophene Ring System

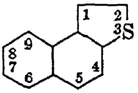
116
156
157
159
161
162
163
166
171
205
307
308
509

P-35
P-41
P-43
P-52
P-56
P-123
P-128
P-154
P-163
P-174
P-212
P-213
P-220

P-228
P-246
P-426
P-456
P-464
P-520
P-602
P-611
P-614
P-616
P-627
P-636
P-653
P-713

V. Naphtho[2,1-*b*]thiophene Ring Systems

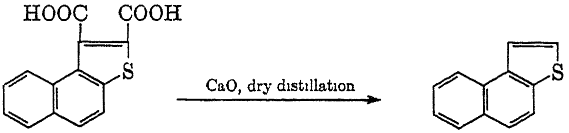
A. Naphtho[2,1-*b*]thiophene



(*Ring Index* No. 1745)

Preferred Name	*Other Names*
Naphtho[2,1-*b*]thiophene	β-Naphthothiophene
	2,1-Naphthothiophene
	Naphtho-2′,1′:2,3-thiophene
	4,5-Benzothionaphthene

Naphtho[2,1-*b*]thiophene (I) has been made by the reduction of 1-hydroxynaphtho[2,1-*b*]thiophene and by the dry distillation of naphtho[2,1-*b*]thiophene-1,2-dicarboxylic acid (II) over lime (378) (eq. 39). It has also been made in 54% yield by cyclizing 2-naphthyl-2-dimethoxyethyl sulfide with a H_3PO_4-P_2O_5 mixture at 150° *in vacuo* (764).



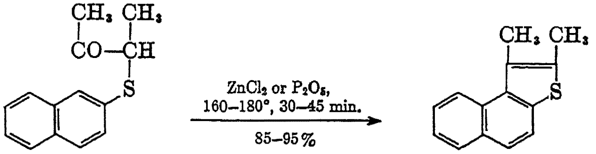
(II) (I)

(39)

The nitration of I with fuming nitric acid in acetic acid leads to a mononitro derivative. On the basis of substitution reactions occurring in the thianaphthene nucleus, it would seem probable that nitration occurs predominantly in the 1-position. Smaller amounts of the 2-isomer would also be expected.

B. Alkyl Derivatives of Naphtho[2,1-*b*]thiophene

1,2-Dimethylnaphtho[2,1-*b*]thiophene has been made by the cyclization of 3-(2′-naphthylthia)-2-butanone (528) (eq. 40). The structure of the

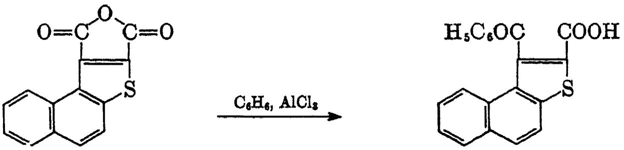


(40)

dimethylthiophene was established by reducing it with Raney Nickel to 1-*sec*-butylnaphthalene.

C. Acids of Naphtho[2,1-*b*]thiophene

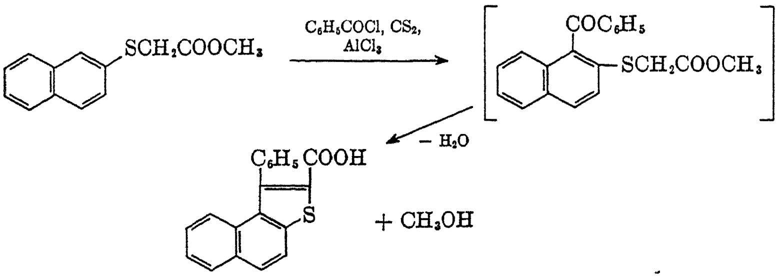
Naphtho[2,1-*b*)thiophene-1,2-dicarboxylic acid (II) is prepared by the method used for the synthesis of thiophanthrenedicarboxylic acid (378) (see eq. 5). In contrast to its thiophanthrene analog, the anhydride of II will acylate benzene in the presence of aluminum chloride (eq. 41). All attempts to cyclize the ketoacid to the quinone were unsuccessful. The position of the benzoyl group was assigned on the basis of the analogous reac-



(41)

tion between thianaphthenedicarboxylic acid anhydride and benzene (see eq. 8, Chapter VI).

1-Phenyl-2-naphtho[2,1-*b*]thiophenecarboxylic acid has been prepared from the methyl ester of 2-naphthylthioglycolic acid and benzoyl chloride (P-474). The transformation probably occurs as shown in eq. 42. This

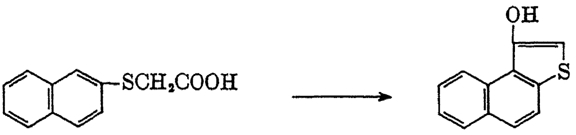


(42)

would seem to be an excellent way of making 1-substituted derivatives of I, since dry distillation of the acid over lime should yield the decarboxylated material.

D. 1-Hydroxynaphtho[2,1-*b*]thiophenes and Derivatives

1-Hydroxynaphtho[2,1-*b*]thiophene (III) has been made by the cyclization of 2-naphthylthioglycolic acid and 1-substituted 2-naphthylthioglycolic acids (P-217,205) (eq. 43). As mentioned previously, 2-naphthylthioglycolic acids on cyclization will usually form the [2,1-*b*] isomer rather than the thiophanthrene derivatives.



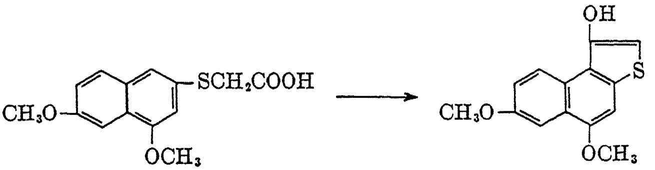
(III)

(43)

III has also been formed in 50% yield by the action of sulfur on 1-acetylnaphthalene (171) and by a series of steps from 1,2-naphthol[2,1-*b*]thiophenequinone (P-503). Both of these methods have been described previously.

A number of polyhydroxy and polyalkoxy naphtho[2,1-*b*]thiophenes have been prepared by previously described methods (308,P-528,P-190, P-94,P-217,P-422,P-452).

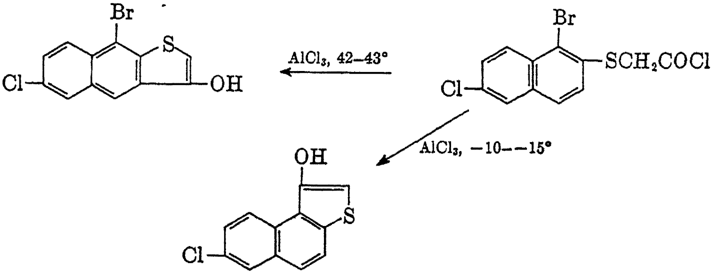
The ring closure of 4,6-dimethoxy-2-naphthylthioglycolic acid yields a material which is probably the [2,1-*b*] isomer (P-452) (eq. 44). Although



(44)

no structure was assigned to the material, it seems probable that cyclization would occur at the more reactive 1-position. The steric hindrance of the methoxy group would also tend to make substitution at the 3-position more difficult.

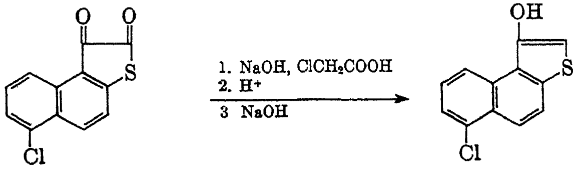
As mentioned in the thiophanthrene section, ring closure of a 1-halogenated-2-naphthylthioglycolic acid leads to the formation of a thiophanthrene with retention of the halogen. Höllze (298) has found that removal of the 1-halogen occurs at lower temperatures (eq. 45). This reaction was carried



(45)

out on the chlorides of 1-bromo-6-chloro, 1,5- and 1,6-dichloro-2-naphthylthioglycolic acids. When attempted with 1-bromo- and 1-chloro-2-naphthylthioglycolic acids, only the thiophanthrene derivatives were formed, indicating that the second halogen must have some activating effect on the one removed. It would be interesting to run this reaction on naphthylthioglycolic acids in which the substituents in the 5- and 6-positions are, alternatively, ortho, para, and meta-directing groups to see whether this activating effect can be attributed to the electron releasing ability of the halogen groupings.

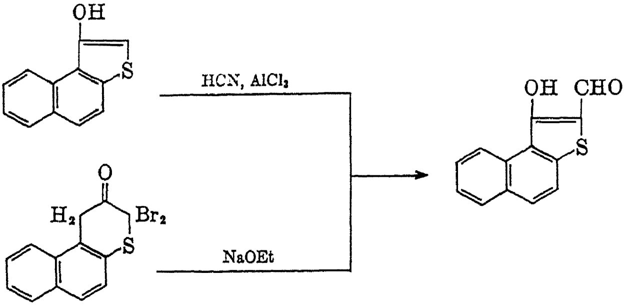
A number of halogenated 1-hydroxynaphtho[2,1-*b*]thiophenes have been prepared as shown in eq. 46 (P-503). This method is also applicable



(46)

to the preparation of the [2,3-*b*] and the [1,2-*b*] isomers. Bromination of 1-hydroxynaphtho[2,1-*b*]thiophene leads to the 2,2-dibromo derivative (P-405,P-506).

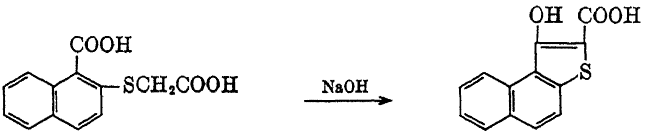
1-Hydroxy-2-naphtho[2,1-*b*]thiophenecarboxaldehyde has been prepared by the conventional Gattermann synthesis and by the action of sodium ethoxide on 1-oxo-2,2-dibromonaphtho-[2,1-*b*]thiapyran (333) (eq. 47). This second method is discussed more fully under the preparation of 3-hydroxy-2-thianaphthenecarboxyladehyde (Chapter II, section IX-A).



(47)

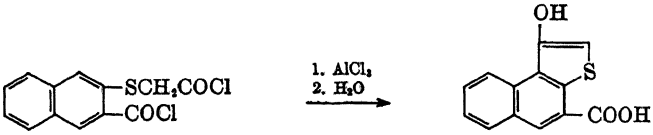
It is noteworthy that this is the only aldehyde to be prepared in the naphthothiophene series. It serves to emphasize further the fact that derivatives of the naphthothiophenes were synthesized primarily because they were dye intermediates. Their other chemical properties and reactions were of secondary importance.

1-Hydroxy-2-naphtho[2,1-*b*]thiophenecarboxylic acid has been isolated as the monohydrate from the careful ring closure of 1-carboxy-2-naphthylthioglycolic acid (205) (eq. 48). This material is very easily decarboxylated and can be oxidized directly to the thioindigo dye.



(48)

1-Hydroxy-4-naphtho[2,1-*b*]thiophenecarboxylic acid has been prepared as shown in eq. 49 (P-460). This is a little surprising since one



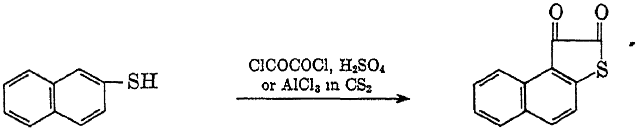
(49)

would have expected the effect of the acid chloride group to be similar to that of the carboxyl group. The presence of a carboxyl group in the 3-position and ortho to the sulfur usually results in cyclization to the thiophanthrene derivative (160). The corresponding 5- and 6-acids have also been prepared in a similar manner (P-222,P-643).

These acids have been condensed with aminoanthraquinones to form vat dyes. Oxidation to the acids leads to the symmetrical naphthothioindigo dyes.

E. 1,2-Naphtho[2,1-*b*]thiophenequinone and Derivatives

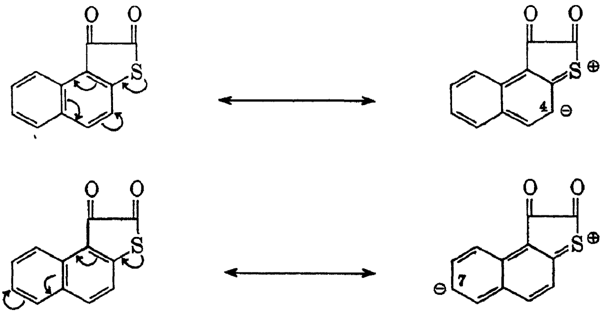
1,2-Naphtho[2,1-*b*]thiophenequinone (IV) has been prepared by reacting oxalyl chloride with 2-mercaptonaphthalene (P-510,P-609,P-610,P-35, P-228) (eq. 50). IV has also been prepared by hydrolysis of the anil formed from nitrosobenzene and 1-hydroxynaphtho[2,1-*b*]thiophene (III) and by refluxing the 2,2-dibromide of III with acetic acid (P-506,P-33).



(IV)

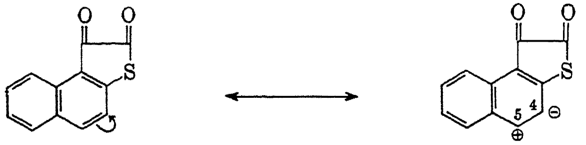
(50)

The only reported substitution reaction of IV is bromination, which leads to a monobromo derivative of undetermined structure (P-56,P-615). In this case, on the basis of electromeric effect alone, there appear to be two positions of almost equal probability where substitution could take place (eq. 51). The primary difference is the proximity of the 4-position to the



(51)

sulfur atom. The inductive effect of the sulfur atom should polarize the double bond in the 4,5-position in the same direction as the electromeric effect (eq. 52). The combination of both effects should favor substitution at



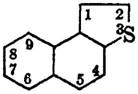
(52)

the 4-position. The only other known bromo derivative, the 6-isomer, has a melting point which is different from that of the derivative obtained by direct bromination (P-611,P-35).

The 6, 7, 8, and 9-monochloro derivatives of IV have been prepared by condensing oxalyl chloride with appropriately substituted naphthylthioglycolic acids (P-611,P-35). 5-Chloro-1,2-naphtho[2,1-*b*]thiophenequinone has been made by the hydrolysis of its 2,2-dibromide. The 4-isomer has not been reported in the literature.

A large number of other derivatives of IV have been prepared by conventional methods and their melting points are listed in Table V-3 (P-587, P-405,P-506,378,205).

TABLE V-3. Melting Points of Naphtho[2,1-*b*]thiophene and Its Derivatives



Substituent	M.p., °C.	Ref.
Naphtho[2,1-*b*]thiophene		
None	108–109	378
—, picrate	116–117	764
	151	764
1,2-Di-CH_3	106–107	525
1-(?)-NO_2	92	378
1-C_6H_5-2-COOH	224–225	P-474
1-C_6H_5CO-2-COOH	275	378
1,2-Di-COOH	276	378
1-OH	121	205
	118–119	P-355
1,7-Di-OH	130–133	308
1,8-Di-OH	92	308
1-OH-8-CH_3O	161–162	P-528
1-OH-5,7-di-CH_3O	196	P-452
	194	P-217
1-OH-5,8-di-CH_3O	165	P-217
1-OH-5-C_2H_5O	121	P-528
1-OH-7-C_2H_5O	142–144	P-528,P-190,P-94
1-OH-5,7-di-C_2H_5O	196	P-452

Substituent	M p., °C.	Ref.
Naphtho[2,1-*b*]thiophene (*continued*)		
1-OH-4-Cl	149–150	P-395
1-OH-6-Cl	146	P-503
1-OH-8-Cl	155	P-503
1-OH-9-Cl	179	P-503
1-OH-6-Br	170	P-503
1-OH-2-CHO	147	333
1-OH-2-COOH·H_2O	69	205
1-OH-4-COOH	>250	P-460,P-222
1-OH-5-COOH	>230	P-460,P-222,P-643
1-OH-6-COOH	>240	P-460,P-222
1-OH-5-CH_3O-7-Cl	209	P-217,P-453
1-OH-5-CH_3O-8-Cl	242	P-217,P-453
1-OH-5-C_2H_5O-7-Cl	203	P-453
1-OH-7-C_2H_5O-6-Cl	240	P-641
1-OC_2H_5-2,4-di-COOH	>250	P-222
1,2-Naphtho[2,1-*b*]thiophenequinone		
None	168	P-35
	153	P-609,P-610
		P-506
2,2-Di-Br	150	P-405,P-506
2-*p*$(CH_3)_2NC_6H_4N$=	228	P-405,P-506
	229-230	378
	224	P-174
2-*p*HOC_6H_4N=	270–275	P-587
2-C_6H_5NHN=	184	378
2-C_6H_5CH=	159	205
2-*p*-$NO_2C_6H_4CH$=	287	205
4-COOH	296–297	P-460
4-COOH-2-*p*$(CH_3)_2C_6H_4N$=	350	P-460
5-Cl	178	P-506
6-Cl	210	P-611,P-35
7-Cl	191	P-611,P-35
8-Cl	204	P-611
9-Cl	207	P-611,P-35
4-(?)-Br	202	P-56,P-615
6-Br	212–213	P-611,P-35

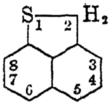
References for Thioindigo Dyes Containing an Unspecified Naphthothiophene Ring System

P-30
P-50
P-454
P-463
P-483
P-570
P-639
P-645

References for Thioindigo Dyes Containing the Naphtho [2,1-*b*]Ring System

158
159
161
162
163
166
171
174
205
307
308
378
P-27
P-29
P-35
P-41
P-52
P-56
P-81
P-85
P-123
P-152
P-156
P-163
P-174
P-194
P-212
P-213
P-217
P-220
P-222
P-228
P-248
P-355
P-397
P-405
P-426
P-436
P-438
P-451
P-462
P-502
P-506
P-574
P-587
P-589
P-602
P-611
P-612
P-613
P-627
P-636
P-641
P-647
P-653

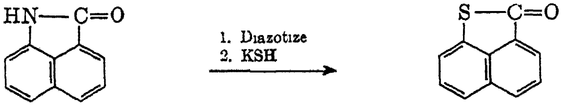
VI. 2*H*-Naphtho[1,8]thiophene



(*Ring Index* No. 1746)

Preferred Name	*Other Name*
2*H*-Naphtho[1,8]thiophene	2-*peri*-Naphthothiophene

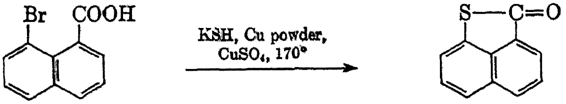
The parent compound in this series is unknown. 2*H*-Naphtho[1,8]thiophene-2-one (I) has been synthesized from naphthostyril (205) (eq. 53).



(53)

(I, m.p. 144.5–145.5°)

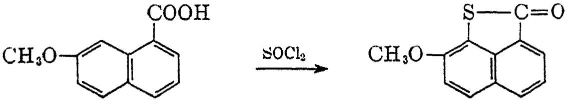
The hydrolysis of I with dilute alkali yields the disodium salt of 1-mercapto-8-naphthoic acid. (I) has also been synthesized from 1-bromo-8-naphthoic acid (434) (eq. 54).



(54)

m.p. 145°

The treatment of 2-methoxy-8-naphthoic acid with thionyl chloride leads to a product which analyzes empirically as 8-methoxy-2-naphtho[1,8]thiophene-2-one (185) (eq. 55).



m.p. 143.5–144°

(55)

VII. Naphtho[1,2-*c*]thiophene

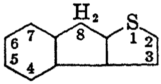
As was mentioned previously in this chapter, this is the only naphthothiophene ring system that has not been synthesized. There are several methods available which should produce this ring system.

The action of either sodium sulfide on 1,2-di(bromomethyl)naphthalene or of hydrogen sulfide on the 1,2-diacid chloride of naphthalene should produce derivatives of this system. The first method has been used to prepare 1,3-dihydroisothianaphthene (67), while the second has been applied to the synthesis of 1,3-naphtho[1,8-*cd*]thiapyranone (500).

It also seems likely that 1- or 2-naphthylmethylmercaptan could be reacted with either phosgene or methylene dichloride to yield the naphtho[1,2-*c*]thiophene ring system. There does not seem to be any theoretical reason for the nonexistence of this system.

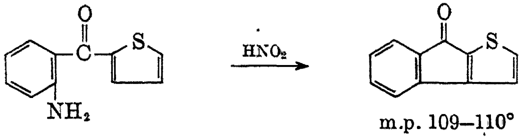
VIII. Miscellaneous Three-Ring Systems Containing One Thiophene Ring

A. 8*H*-Indeno[2,1-*b*]thiophene Ring System



(*Ring Index* No. 1447)

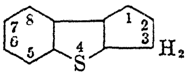
8*H*-Indeno[2,1-*b*]thiophene-8-one has been isolated in low yields as a by-product from the diazotization and coupling of 2-aminophenyl-2′-thienyl ketone (476) (eq. 56). The major product of this reaction is 2-hydroxyphenyl-2′-thienyl ketone.



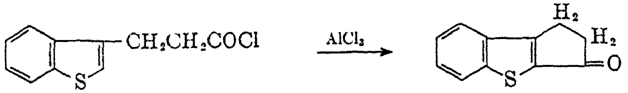
m.p. 109–110°

(56)

B. 3*H*-Cyclopenta[*b*]thianaphthene Ring System



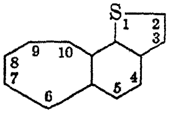
3*H*-1,2-Dihydrocylopenta[*b*]thianaphthene-3-one has been made by the cyclization of 3-(3′-thianaphthenyl)propionyl chloride (90) (eq. 57). This material undergoes the Pfitzinger reaction with isatin.



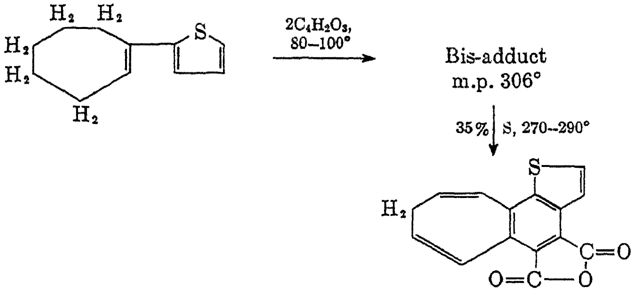
m.p. 161°
Semicarbazone, m.p. 304°

(57)

C. 8*H*-Cyclohepta[*g*]thianaphthene Ring System



The dicarboxylic anhydride of 8*H*-cyclohepta[*g*]thianaphthene has been made by adding maleic anhydride to 1-(2′-thienyl)cycloheptene-1 and dehydrogenating the adduct with sulfur (537) (eq. 58). As was the case with



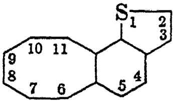
m.p. 255–256°

(58)

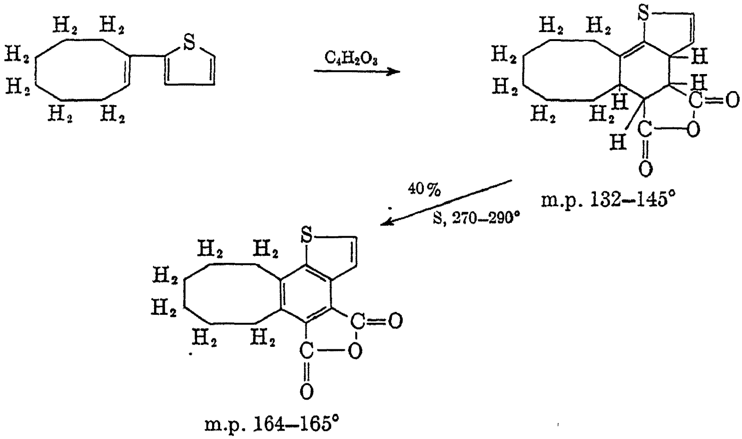
the thienyl cyclohexenes, a bis adduct involving two moles of maleic anhydride was formed. The double bonds in the cycloheptatriene ring were assumed to be in conjugation with the aromatic portion of the molecule.

Note added in proof: 3*H*-1,2,4,5-Tetrahydrocyclohepta[*b*]thianaphthene (m.p. 71.5°) and several of its derivatives have been reported recently (782). The synthesis involves an initial condensation of glutaric anhydride with thianaphthene followed by the usual sequence of reduction and cyclization reactions.

D. Cycloocta[*g*]thianaphthene Ring System



3a,4,5,5a,6,7,8,9,10,11 - Decahydrocycloocta[*g*]thianaphthene - 4,5 - dicarboxylic anhydride has been made by reacting maleic anhydride with 1-(2′-thienyl)cyclooctene-1 (537) (eq. 59). In contrast to cases discussed previously, only a mono adduct was formed. Dehydrogenation of this adduct yielded the 6,7,8,9,10,11-hexahydro derivative. Attempts to dehydrogenate the cyclooctene ring completely were unsuccessful.



(59)

CHAPTER VI

Thiophene Systems Containing Three or More Carbocyclic Fused Rings

I. Introduction

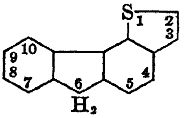
Very little is known of the chemistry of these polycyclic systems. A fairly large number of ring systems of this type have been prepared, but there are only isolated cases in which substitution reactions are reported. In many cases the parent ring systems have not been prepared and only the synthesis of a single derivative is reported.

The one ring system in this section that has been studied fairly extensively is the benzo[*b*]thiophanthrene system. Most of the interest has been centered on 6,11-benzo[*b*]thiophanthraquinone and its derivatives, since these materials are easily prepared and are also good dye intermediates. Even in this case, there are no reported reactions of the parent compound, benzo[*b*]thiophanthrene, in spite of the fact that it has been synthesized by five different methods.

The ring systems in this section are discussed in the order that they would be expected to appear in *Ring Index*. Only the melting points of benzo[*b*]thiophanthrene and its derivatives appear in table form. Melting points of other compounds are listed in the text.

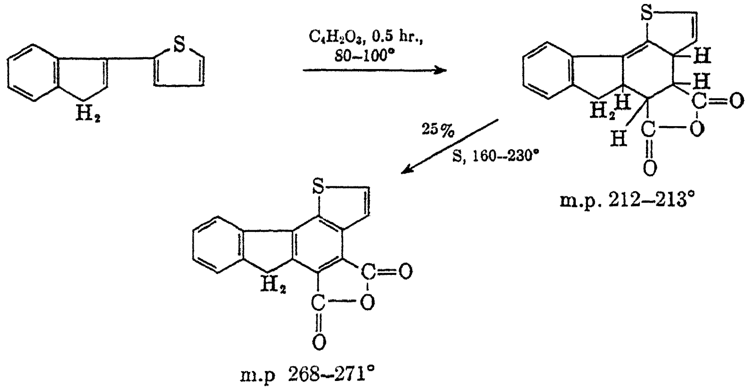
II. Four Ring Systems

A. 6*H*-Indeno[2,1-*f*]thianaphthene



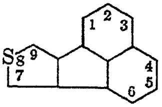
$C_{15}H_{10}S$

The 4,5-dicarboxylic anhydride of this system has been made by reacting 3-(2′-thienyl)-indene with maleic anhydride followed by dehydrogenation with sulfur (537) (eq. 1). The intermediate tetrahydro derivative is obtained as a mono adduct rather than as a bis adduct which forms with 1-(2′-thienyl)cyclohexene.



(1)

B. Acenaphtheno[1,2-*c*]thiophene

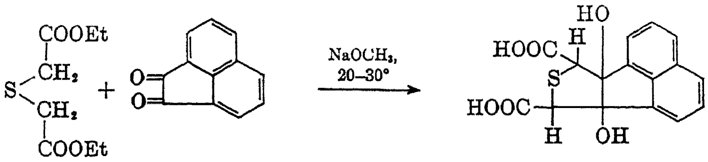


$C_{14}H_8S$

(*Ring Index* No. 2312)

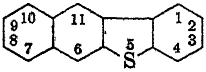
Other Names
Acenaphthoisothiophene
7,8-β-acenaphthothiophene

6b,7,9,9a-Tetrahydro-6b,9a-dihydroxy-7,9-acenaphtho[1,2-*c*]thiophenedicarboxylic acid has been made by reacting acenaphthenequinone with ethyl thiodiglycolate (293) (eq. 2). This is a colorless material decomposing at 250° with loss of water and carbon dioxide.



(2)

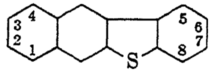
C. Benzo[*b*]thiophanthrene



$C_{16}H_{10}S$

(*Ring Index* No. 2502)

Other Numbering

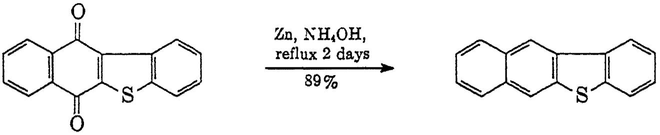


Other Names

Benzothiophanthracene
β-Thiobrazan

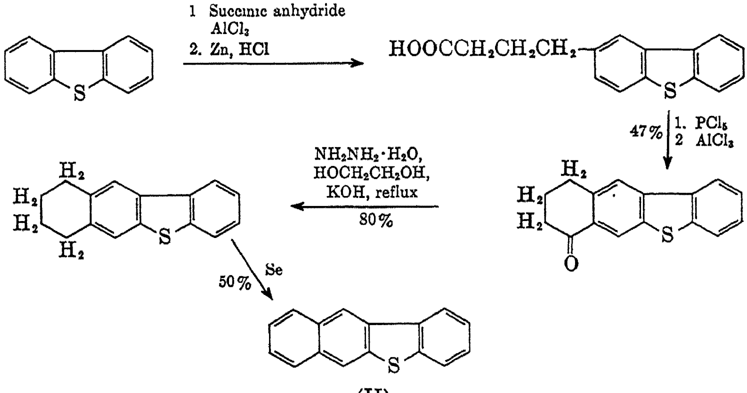
1. *Benzo[b]thiophanthrene*

The first and probably one of the best methods for the preparation of this material involves reduction of 6,11-benzo[*b*]thiophanthraquinone (I) with zinc dust (378) (eq. 3). Heating of I with zinc dust in a combustion tube in the presence of a stream of hydrogen is also reported to yield II (331).

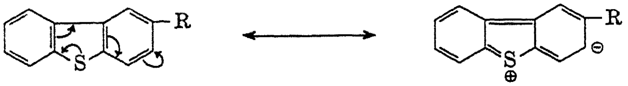


(I) (II) (3)

II has been prepared from dibenzothiophene and succinic anhydride by the following series of reactions (526,77) (eq. 4). Ring closure occurs at the 3-position rather than the 1-position of the dibenzothiophene nucleus. This would be the predicted position based on the resonating structures shown in eq. 5.

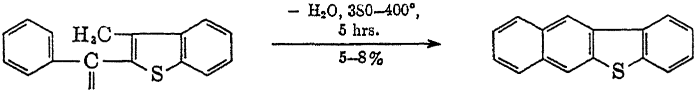


(II) (4)



(5)

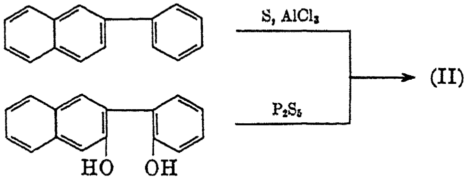
II has also been synthesized in low yields from 2-benzoyl-3-methylthianaphthene (526) (eq. 6).



(II)

(6)

Kruber and Rappen (337) have demonstrated the presence of II in the chrysene portion of coal tar. They were also able to synthesize II by methods previously used for the synthesis of dibenzothiophene. No yields were given (eq. 7).



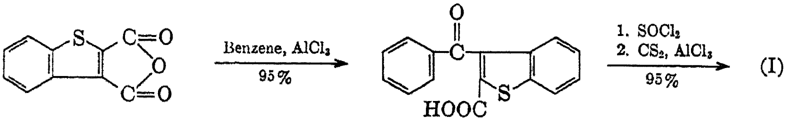
(7)

2. *6,11-Benzo[b]thiophanthraquinone and Derivatives*

The most widely studied material in this chapter is 6,11-benzo[*b*]thiophanthraquinone (I), or benzothiophanthraquinone, as it is more commonly called. Interest in this substance stems from the fact that it is a dye, coloring wool yellow from an alkaline vat, and that it is also an intermediate for other faster dyes.

Most of the syntheses of I have been achieved by the cyclization of ortho keto acids involving the thianaphthene and benzene nuclei; all four possible combinations of this type have been synthesized and cyclized to yield I.

2,3-Thianaphthenedicarboxylic anhydride can be condensed with benzene to form 3-benzoyl-2-thianaphthenecarboxylic acid which can be cy-

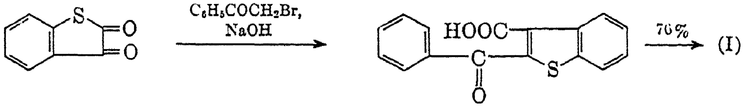


(III)
m.p. 215–216°

(8)

clized to yield the quinone (378,P-70,P-523) (eq. 8). It should be noted that ring opening occurs, to yield a benzoyl group attached to the 3-position of thianaphthene.

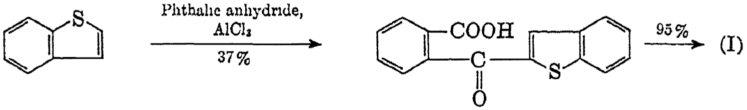
The proof of structure of III consisted of synthesizing the only other possible 2,3-benzoylthianaphthenecarboxylic acid (IV) from phenacyl bromide and 2,3-thianaphthenequinone and showing that it was different from III (eq. 9). The mechanism of the formation of compounds such as IV has been previously discussed.



(9)

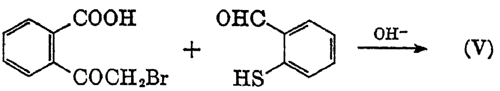
(IV)
m.p. 240–241°

I has also been prepared by the condensation of phthalic anhydride and thianaphthene (378,P-416,P-68,P-540,P-415) (eq. 10). The intermediate product, 2-(2′-thianaphthenoyl)benzoic acid (V) is unexpected, since electrophilic substitution usually occurs predominantly at the 3-position of thianaphthene. The structure of V was established by independent synthesis (eq. 11). The acid obtained by this method was identical with the acid obtained from phthalic anhydride and thianaphthene. Although this appears to be substantial proof for the structure of V, an earlier patent by Mayer (P-523) cites the formation of 2-(3′-thianaphthenoyl)benzoic acid from phthalic anhydride and thianaphthene. No supporting evidence was presented in this case.



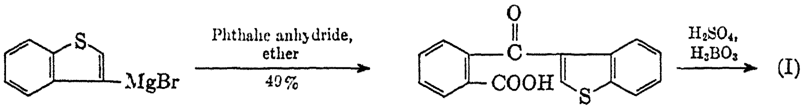
(10)

(V)
m.p. 175°



(11)

The fourth acid (VI) prepared by reacting phthalic anhydride with 3-thianaphthenylmagnesium bromide has also been cyclized to yield I (331) (eq. 12). It is interesting to note that the methyl esters of V and VI have identical melting points.

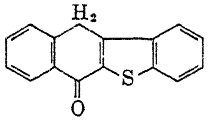


(12)

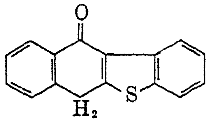
(VI)
m.p. 150.5–151.5°

I has also been made by the chromic acid oxidation of benzo[*b*]thiophanthrene (77,378).

Very few reactions have been carried out on 6,11-benzo[*b*]thiophanthraquinone. As mentioned previously, reduction in the presence of zinc yields benzo[*b*]thiophanthrene (378,331). Reduction with sulfurous acid, however, leads to the formation of a material which analyzes as benzo[*b*]thiophanthrone. This material could not be crystallized and is believed to be a mixture of the two possible benzothiophanthrones (A and B).



(A)

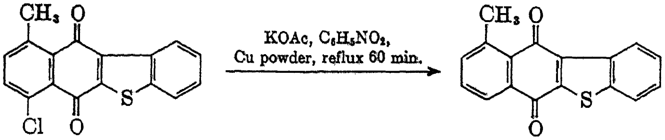


(B)

The reaction of bromine with I forms a dibromo derivative (331). Fusion of this material with alkali yields a dihydroxy derivative.

The reaction of I and glycerine to yield 7*H*-dibenzo[*b*,*ef*]thiophanthrene is discussed in the next section (754,378,P-540,P-43,P-68).

A fairly large number of derivatives of benzothiophanthraquinone has been prepared. Almost all of the syntheses involve ring closure of an intermediate *o*-keto acid. The methods used for the syntheses of the intermediates are similar to those described under the preparation of the parent compound. For example, 8-methylbenzothiophanthraquinone has been made by reacting 2,3-thianaphthenedicarboxylic anhydride with toluene. As was mentioned previously, the initial ring rupture occurs next to the carbonyl group attached at the 3-position of thianaphthene. The 9-methyl derivative has been made by reacting *p*-methylphenacyl bromide with thianaphthenequinone. The 10-methylbenzothiophanthraquinone has been synthesized by reacting 2,3-thianaphthenedicarboxylic anhydride with *p*-chlorotoluene followed by removal of the chloro group (eq. 13). Although

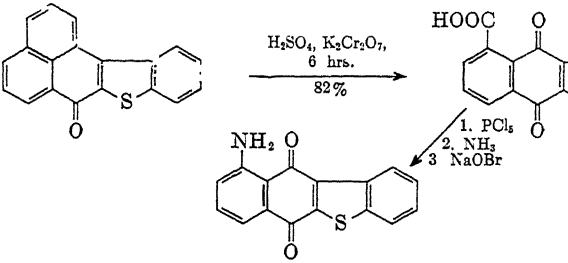


(13)

the author did not assign a position to either the chloro or methyl grouping, it seems probable that the initial acylation would take place predominantly *ortho* to the methyl group. This would yield the 7-chloro-10-methyl derivative, which on subsequent reduction is converted to 10-methylbenzothiophanthraquinone.

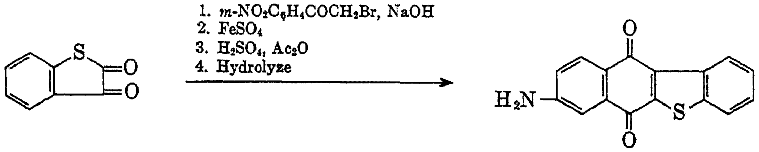
Both the 8-chloro- and 8-bromobenzothiaphanthraquinones have been synthesized by reacting 2,3-thianaphthenedicarboxylic anhydride with the respective halobenzene followed by cyclization. An attempt to prepare the methoxyl derivative by this procedure was unsuccessful, since cyclization of the intermediate 3-(4′-methoxybenzoyl)thianaphthene-2-carboxylic acid could not be effected.

The 10-aminobenzothiophenanthraquinone has been prepared from 7*H*-dibenzo[*b*,*ef*]thiophanthrene-7-one (equation 14) (378). Mayer could not decide whether the carboxyl or amino groups were in the 7- or 10-positions, since the structure of the starting material was uncertain. Later work on the structure study of 7*H*-benzo[*ef*]thiophanthrene (754) indicates that the above structure is correct and that the derivatives are substituted in the 10-position. This work is discussed in greater detail under 7*H*-benzo[*ef*]thiophanthrene and 7*H*-dibenzo[*b*,*ef*]thiophanthrene.

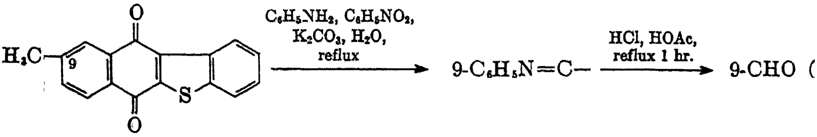


(14)

The only other monoamino derivative, 8-aminobenzothiophanthraquinone, has been prepared according to eq. 15. The 9-substituted aldehyde



(15)



(16)

derivative of I has been made by a series of interesting reactions (378) (eq. 16). The 9-methyl derivative is probably oxidized by the nitrobenzene to the aldehyde, which then reacts with aniline to form the anil. Hydrolysis of the anil yields the aldehyde. The 8-anil was also made in this fashion, but there is no mention of its hydrolysis to the aldehyde.

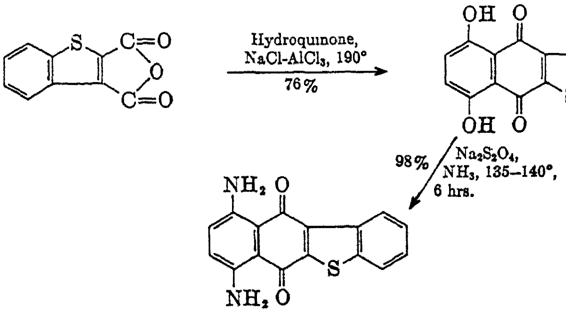
A number of polysubstituted benzothiophanthraquinones have been prepared by the following general methods:

(*1*) Reaction of a polysubstituted thianaphthene with phthalic anhydride (378,417).

(*2*) Reaction of a polysubstituted thianaphthenedicarboxylic anhydride with benzene (378,P-68).

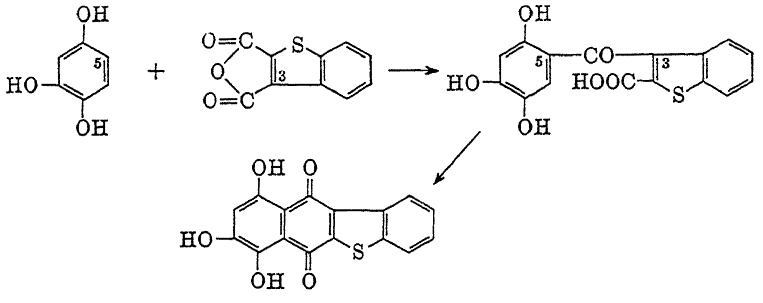
(*3*) Reaction of a thianaphthenedicarboxylic anhydride with a disubstituted benzene (378,P-527,P-631,P-421,P-93,P-68).

7,10-Dihydroxybenzothiophanthraquinone, synthesized by method 3, possesses fairly labile hydroxyl groups, since they can be converted almost quantitatively to amino groups (eq. 17). Under more mild conditions, 75–90°, only one hydroxyl is replaced. The positions of the amino and hydroxyl groups were not determined.



(17)

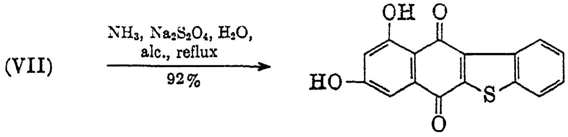
The reaction between thianaphthenedicarboxylic anhydride and hydroxyhydroquinone is described in the literature as yielding a trihydroxybenzo[*b*]thiophanthraquinone, which is either the 7,8,10- or 7,9,10-derivative (378,P-68,P-527,P-631). Since it has been shown that the anhydride tends to form the 3-thianaphthenoyl derivative during acylation and since the 5-position of the hydroxyhydroquinone is the only position activated by both an *ortho* and *para* hydroxyl group, it appears likely that the reaction would proceed according to eq. 18 to form the 7,8,10-derivative (VII). The oxidation of 7,10-dihydroxybenzo[*b*]thiophanthraquinone with lead tetraacetate also yields the same trihydroxy derivative.



(VII)

(18)

The reduction of VII yields a dihydroxy derivative which is probably the 8,10-derivative (eq. 19). It was shown to be different from the 7,10-dihydroxy material and the only other dihydroxy derivative, the 7,8-derivative, was not considered likely to form.

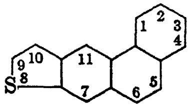


(19)

A more rigorous structure proof would consist of synthesizing the 8,10-derivative by reacting thianaphthenedicarboxylicanhydride and resorcinol. Again, it should be emphasized that the structures of these materials are based on the premise that ring opening occurs to form a carbonyl group in the 3-position of thianaphthene.

A fairly large number of other substituted benzo[*b*]thiophanthraquinones have been prepared and are listed in Table VI-1, p. 324

D. Benzo[*g*]thiophanthrene



$C_{16}H_{10}S$

Other Name

5,6-Benzothiophanthrene

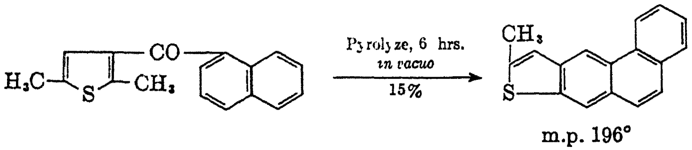
The parent compound, benzo[*g*]thiophanthrene, has not been reported in the literature. 9-Methylbenzo[*g*]thiophanthrene has been prepared by

TABLE VI-1. Melting Points of Compounds Having a Benzo[*b*]thiophanthrene Ring System

Substituents	M.p., °C.	Ref.	Deriv	M.p., °C.	Ref.
		Benzo[*b*]thiophanthrene			
None	163	77	Picrate	128–129	331
	159–160	331,526	5,5-Dioxide	261–262	526
	154–155	378	—	231	337
7,8,9,10-Tetrahydro	110.5–111	526			
	109	77			
7,8,9,10-Tetrahydro-7-one	178–179	526,231	Semicarbazone	280–282	77
	175	77	Oxime	212–213	77
		6,11-Benzo[*b*]thiophanthraquinone			
None	212–213	378,P-523,P-416,P-68,P-540,331,415	Dibromide	270	331
	208–209	77			
8-CH_3	216	378			
9-CH_3	207–208	378,P-439			
10(?)-CH_3	165–166	378			
8-Cl	215–220	378,P-68			
8-Br	225	378			
1-CH_3-3-Cl	272	378,P-417			
	278	P-540			

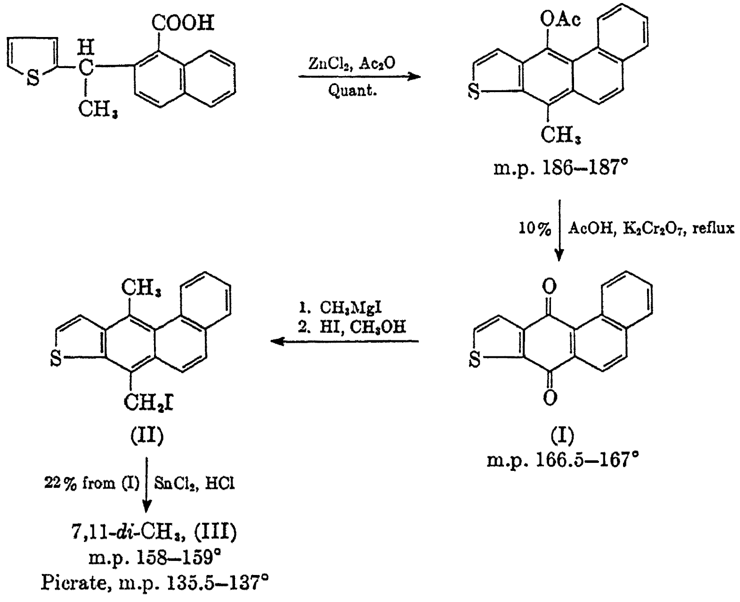
Substituents	M.p., °C.	Ref.	Deriv.	M.p., °C.	Ref.
6,11-Benzo[*b*]thiophanthraquinone					
4-CH_3-2-Cl	304–305	378			
	278	P-68			
10(?)-CH_3-7(?)-Cl	217	378			
1-CH_3-3,8-Di-Cl	215–220	P-540			
4,8-Di-CH_3-2-Cl	262–263	378			
8,10-Di-CH_3-7-Cl	254–255	378			
8-NH_2	302–304	378	Acetyl	343–345	378
10-NH_2	255	378			
7,10-Di-NH_2	305–306	378			
7,10-Di-OH	253–254	378,P-527	Diacetyl	236–237	378
		P-631		235	P-421
	270	P-421			
4-CH_3-2-Cl-7,10-di-OH	291–292	P-631,378,P-527			
8,10-Di-OH	292–293	378			
7,8,10-Tri-OH	241–242	P-68,P-527,P-631,378			
7-NH_2-10-OH or 10-NH_2-7-OH	275–276	378			
8-CHO	—	—	$C_6H_5N=$	203–204	378
9-CHO	257–258	378	$C_6H_5N=$	227	378
			Hydrazide	355	378
10-COOH	278	378	Chloride	275	378
			Amide	257–258	378
			1-Aminoanthraquinone	>360	378

means of the Elbs reaction from 2,5-dimethyl-3-(1′-naphthoyl)thiophene (81) (eq. 20). This material is straw colored and gives a blue-violet fluores-



(20)

cence to benzene or alcohol solutions. It has much less active carcinogenic-activity than the 7,11-dimethyl derivative. 7,11-Dimethylbenzo[*g*]thiophanthrene has been synthesized according to eq. 21 (438). III is reported



(II)

(I)
m.p. 166.5–167°

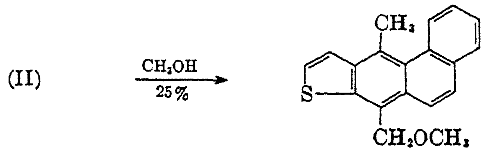
7,11-*di*-CH₃, (III)
m.p. 158–159°
Picrate, m.p. 135.5–137°

(21)

to be highly carcinogenic (152). The quinone (I) colors concentrated sulfuric acid brownish-purple and forms an orange-yellow vat.

I has also been prepared from 2-(2′-thenyl)-1-naphthoic acid by the method described for the preparation of 7,11-benzo[*i*]thiophanthraquinone (439) (see eq. 24).

A material believed to be 11-methyl-7-methoxymethylbenzo[*g*]thiophanthrene was isolated in low yield from the reaction mixtures formed during the conversion of I to the 11-methyl-7-iodomethyl derivative. This material could form from the reaction of methanol with the iodomethyl derivative (eq. 22). This was actually shown to be the case by reacting

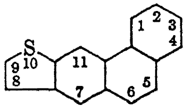


m.p. 121–122°

(22)

the iodomethyl derivative with methanol and converting it to an ether of the same melting point and mixed melting point. The positions of the iodomethyl and methoxymethyl groups were assigned on the basis of results obtained in the benzanthracene series.

E. Benzo[*i*]thiophanthrene

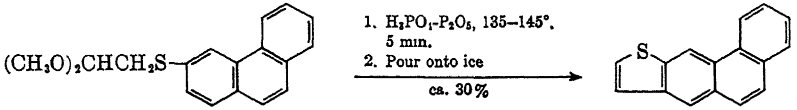


$C_{16}H_{10}S$

Other Name

7,8-Benzothiophanthrene

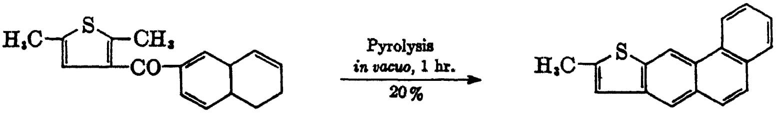
Benzo[*i*]thiophanthrene has been prepared by Tilak (766), who cyclized 3-phenanthryl 2-dimethoxyethyl sulfide by means of polyphosphoric acid (eq. 22A).



(22A)

m.p. 81–82°
Picrate, m.p. 154–155°

9-Methylbenzo[*i*]thiophanthrene has been prepared by the pyrolysis of 2,5-dimethyl-3-(2′-naphthoyl)thiophene (81) (eq. 23).

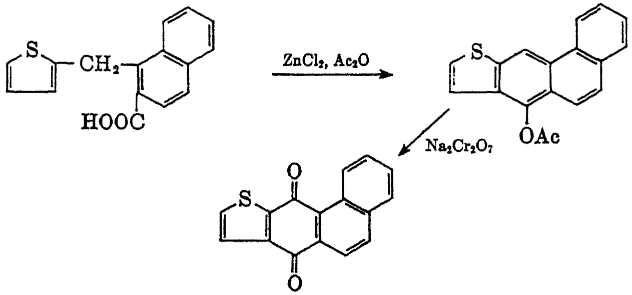


(23)

m.p. 189°

7,11-Dimethylbenzo[*i*]thiophanthrene, m.p. 99–100° (trinitrobenzene complex, m.p. 165°), has been made in 20% yield from 7,11-benzo[*i*]thiophanthraquine (439,438). The preparation is identical to the one used for 7,11-dimethylbenzo[*g*]thiophanthrene (see eq. 21).

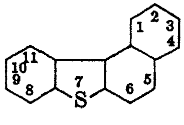
The synthesis of 7,11-benzo[*i*]thiophanthraquinone (I) is complicated by the fact that the cyclization of 1-(2′-thenoyl)-2-naphthoic acid leads to a mixture of the benzo[*i*]- and benzo[*g*]thiophanthraquinones (438,439). This is also true of the 2-(2′-thenoyl)-1-naphthoic acids. These quinones are difficultly separable. This difficulty has been circumvented by first reducing the carbonyl grouping. The 1-(2′-thenyl)-2-naphthoic acid yields only one isomer on cyclization (eq. 24). The overall yield of I is 18%. I has also been prepared by the oxidation of the parent compound, benzo[*i*]thiophanthrene (766).



(I)
m.p. 202–204°

(24)

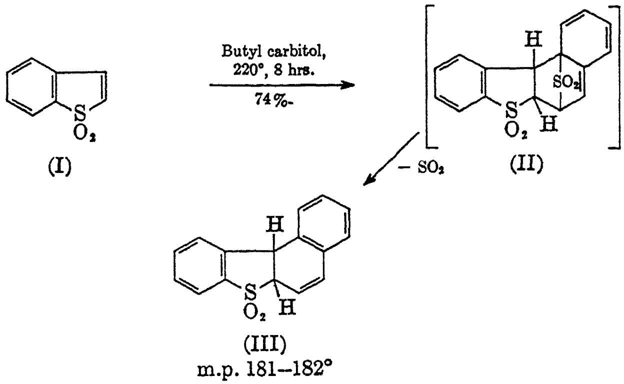
F. Naphtho[2,1-*b*]thianaphthene



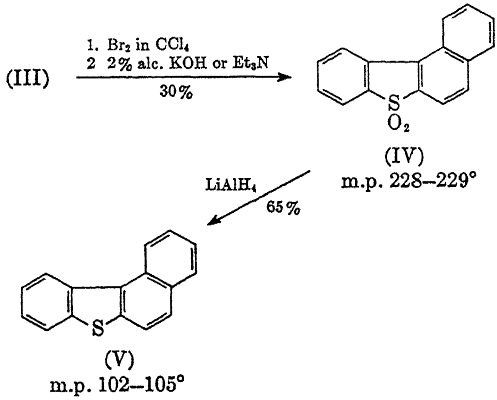
$C_{16}H_{10}S$

Other Name
3,4-Benzo-9-thiafluorene

Naphtho[2,1-*b*]thianaphthene has been synthesized recently in a novel manner (733). When thianaphthene 1-dioxide is heated to temperatures slightly above 200°, loss of sulfur dioxide occurs and III is formed (eq. 25). III reacts with bromine to form a dibromide, which on treatment with potassium hydroxide loses two molecules of hydrogen bromide to give the completely aromatized sulfone (IV). Reduction of IV with lithium aluminum hydride yields naphtho[2,1-*b*]thianaphthene (V) (eq. 26).



(I) (II) (III) m.p. 181–182° (25)



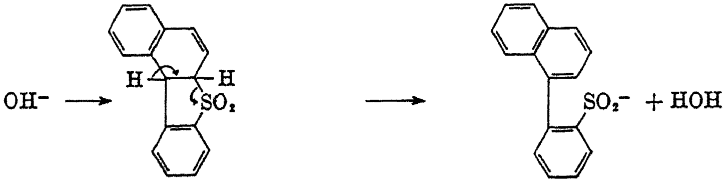
(III) (IV) m.p. 228–229° (V) m.p. 102–105° (26)

Note added in proof: Davies and coworkers (783,784) have indicated more recently that at temperatures of 195–200°, I can be converted directly to V. The latter was also prepared from the maleic anhydride adduct of 1-(3′-thianaphthenyl)cyclohexene by the method described in eq. 27, Chapter V.

The conversion of I to II may be considered to proceed by means of a Diels-Alder reaction. Diels-Alder reactions involving a double bond of a single benzenoid system are not common. However, in this case the loss of sulfur dioxide from II can produce the necessary favorable shift in equilibrium.

A naphtho[1,2-*b*]thiophene derivative could also form in this diene condensation. The configuration of III was proved by desulfurizing it with Raney nickel and dehydrogenating the product to 1-phenylnaphthalene. Degradation of the naphtho[1,2-*b*]thiophene derivative would have yielded 2-phenylnaphthalene.

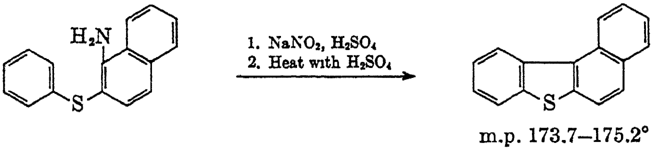
The treatment of III with alcoholic potassium hydroxide produces a rapid elimination reaction to yield potassium *o*-(1-naphthyl)benzenesulfin-



(27)

ate. The mechanism of eq. 27 was postulated. Hydrogenation of III in the presence of a palladium on charcoal catalyst yielded 5,6,6a,11b-tetrahydronaphtho[2,1-*b*]thiophene 7-dioxide (m.p. 183–184°). Hydrolysis of this material with potassium hydroxide yields potassium *o*-(3,4-dihydro-1-naphthyl)benzenesulfinate.

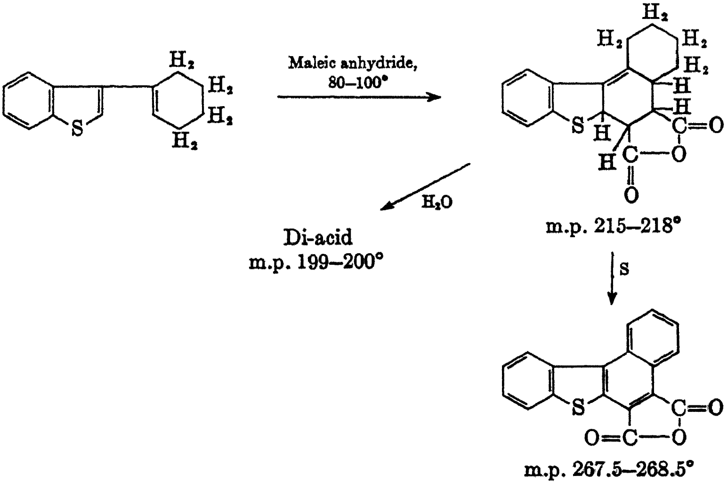
Some naphtho[2,1-*b*]thianaphthene is probably present in the mixture obtained by running the Pschorr reaction on phenyl 1-amino-2-naphthyl sulfide (395) (eq. 28). The sulfur analysis of this material was low and it



(28)

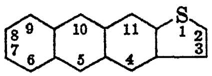
undoubtedly contained some oxidation products. An attempt to make the 10-methyl derivative by this method also yielded a mixture of materials.

5,6-Naphtho[2,1-*b*]thianaphthenedicarboxylic anhydride has been made by the reaction of 1-(3′-thianaphthenyl)-1-cyclohexene with maleic anhydride (537) (eq. 29).



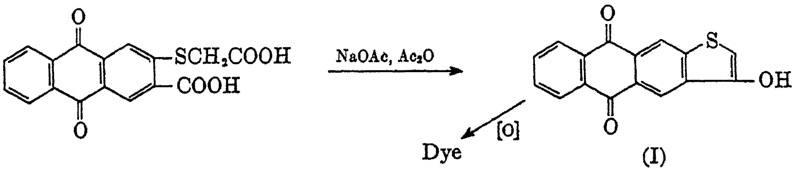
(29)

G. Anthra[2,3-*b*]thiophene



$C_{16}H_{10}S$

Symmetrical dyes which presumably contain the above basic ring system have been made by the oxidation of 3-hydroxy-5,10-anthra[2,3-*b*]thiophenequinone (I) (P-173,P-32,P-254) (eq. 30). I is a brown powder which

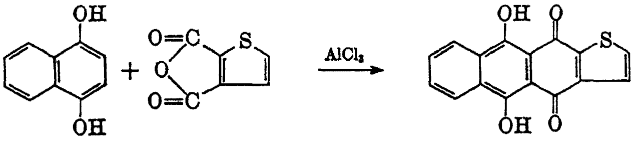


(I)

(30)

couples with arylnitroso compounds to form anils. It also forms a bluish-red color in sulfuric acid. Coupling with isatin yields a dye which tints cotton blue. The symmetrical dye imparts a green shade to cotton.

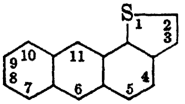
2,3-Thiophenedicarboxylic anhydride has been condensed with materials such as 1,4-dihydroxynaphthalene to yield products which contain the anthra[2,3-*b*]thiophene ring system (P-93) (eq. 31). The preparations of a number of methyl and chloro derivatives of II are also described.



(II)

(31)

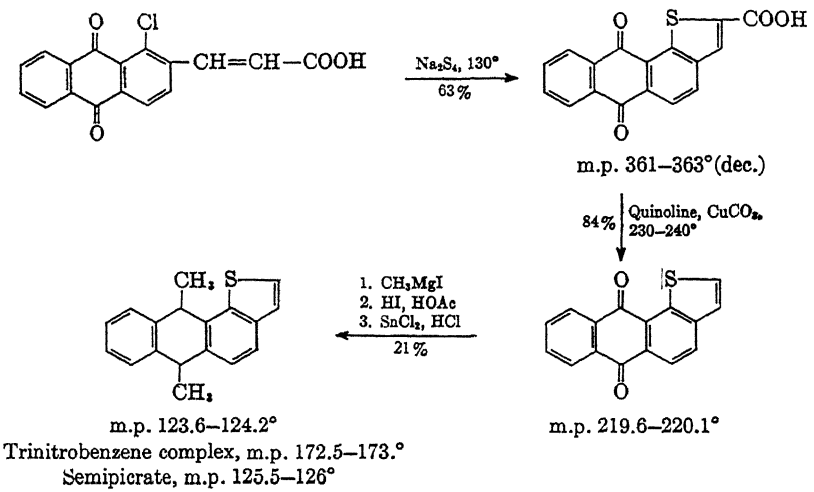
H. Anthra[1,2-*b*]thiophene



(*Ring Index* No. 2503)

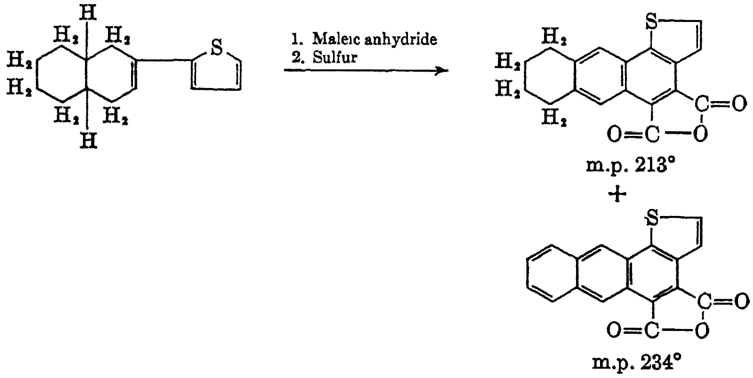
$C_{16}H_{10}S$

The highly carcinogenic 6,11-dimethylanthra[1,2-*b*]thiophene (288) has been synthesized from 2-carboxy-6,11-anthra[1,2-*b*]thiophenequinone (eq. 32). The synthesis of the acid had been described previously (P-578).



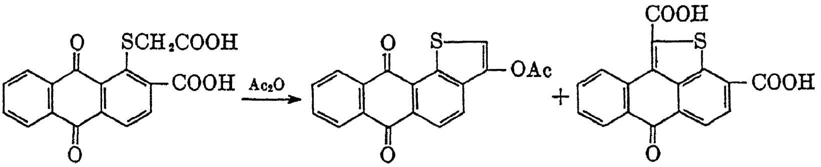
(32)

Anthra[1,2-*b*]thiophene-4,5-dicarboxylic anhydride has been prepared by dehydrogenation of the maleic anhydride adduct of 2-(2′-thienyl)-1,4,-5,6,7,8,9,10-octahydronaphthalene (537) (eq. 33). In the dehydrogenation step a small amount of material, which was incompletely aromatized, was isolated. The structure proposed for this material was the 7,8,9,10-tetrahydro derivative.



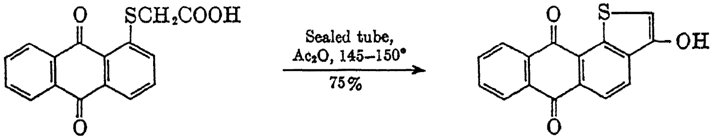
(33)

The cyclization of 2-carboxyanthraquinone-1-thioglycolic acid produces a variety of products depending on the conditions used (P-438,P-259,-P-435,P-436,P-622,P-208,P-433). With acetic anhydride under mild conditions, both II and III are obtained (eq. 34). II and III can be separated easily by treatment with alkali.



(I) (II) m.p. 248° (III) (34)

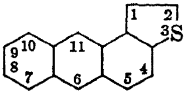
The hydrolysis of II yields the hydroxy derivative (IV). IV can be prepared directly by heating I in trichlorobenzene. A French patent describes the direct formation of IV (m.p. 200°) from I using acetic anhydride as the condensing agent (P-255). IV and the 5-methoxy derivative of IV, m.p. 202–203°, have been prepared according to eq. 35 (227). IV colors sulfuric acid blue-red and forms a symmetrical thioindigo type dye which shades cotton brownish-yellow. A number of other unsymmetrical thioindigo dyes containing the anthra[1,2-*b*]thiophene ring system have been prepared (P-255,P-582,P-622,P-507).



(35)

(IV)
m.p. 179–180°

I. Anthra[2,1-*b*]thiophene



$C_{16}H_{10}S$

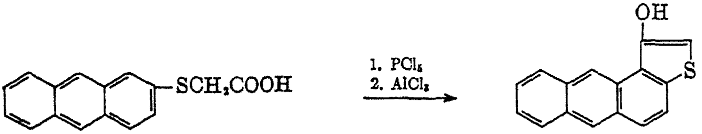
(*Ring Index* No. 2504)

Other Name

3,2-α-anthrathiophene

1-Hydroxyanthra[2,1-*b*]thiophene (I) has been made from anthracene-2-thioglycolic acid (P-57,P-513,P-412) (eq. 36).

I reacts with *p*-nitrosodimethylaniline to form an anil and gives a yellow coloration to sulfuric acid. It also forms a symmetrical thioindigo dye which colors cotton Bordeaux red (P-255).



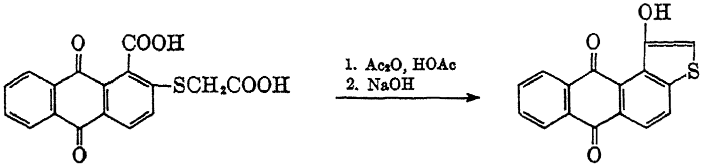
(I)
m.p. 172°

(36)

Cyclization of 1-carboxyanthracene-2-thioglycolic acid with acetic anhydride yields the acyloxy derivative which, on hydrolysis, forms I (P-622).

2-Anthracenethiol has been condensed with oxalyl chloride in the presence of aluminum chloride to form 1,2-anthra[2,1-*b*]thiophenequinone (m.p. 212°) (P-255). This quinone is blue-violet and has been reacted with a number of materials having active hydrogens to form dyes.

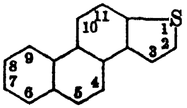
1-Hydroxy-6,11-anthra[2,1-*b*]thiophenequinone (II) has been made by the sequence of reactions illustrated in eq. 37 (433). II forms a benzylidene derivative with benzaldehyde (m.p. 257–261°) and dyestuffs with isatin (m.p. 290° (dec.)), acenaphthaquinone (m.p. 320° (dec.)), and thianaphthenequinone (m.p. 360° (dec.)). These compounds are not technically useful as dyes due to their lack of fastness for cotton and their poor shade of color. Dyes having this ring system and containing different nuclear substituents have also been made (P-134).



(II)
m.p. 230–240°
Acetyl ester, m.p. 154°
p-Bromobenzoyl ester, m.p. 228°

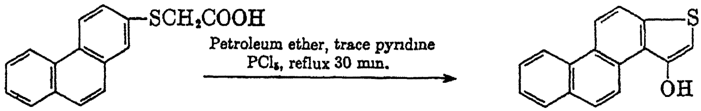
(37)

J. Phenanthro[2,1-*b*]thiophene



$C_{16}H_{10}S$

3-Hydroxyphenanthro[2,1-*b*]thiophene (I) has been prepared according to eq. 38 (702). Ring closure is expected at the 1-position in preference to



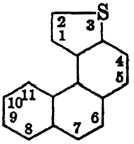
(I)

(38)

the 3-position, since the cyclization of 3-(2′-phenanthryl)propionic acid is known to occur at the 1-position. I was not isolated in pure form, but it was oxidized with potassium ferricyanide to the symmetrical, chocolate thioindigo dye, m.p. 197–198°. I could also be condensed with phenanthroquinone, acenaphthaquinone, and isatin to form high melting, violet dyes.

2,3-Phenanthro[2,1-*b*]thiophenequinone (II) (m.p. 232°) has been made by condensing 2-mercaptophenanthrene with oxalyl chloride (703). Condensation of II with *o*-phenylenediamine yielded the expected quinoxaline, m.p. 274°. II was also condensed with 2,3-diaminoquinoxaline and 2,3-diaminophenazine to yield quinoxalines melting at 230 and >290°.

K. Phenanthro[3,4-*b*]thiophene



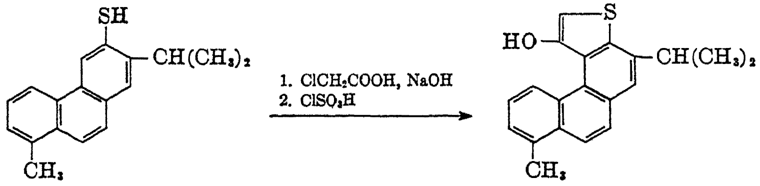
$C_{16}H_{10}S$

(*Ring Index* No. 2505)

1-Hydroxyphenanthro[3,4-*b*]thiophene (I) has been synthesized by the cyclization of 3-phenanthrenethioglycolic acid (702). As in the previous section, the position at which cyclization occurred was assigned on the basis of the known orientation of 3-(3′-phenanthryl)propionic acid. I was not isolated, but was oxidized to the violet, symmetrical thioindigo dye, m.p. 226°. Condensation of I with phenanthraquinone, acenaphthaquinone, and indole yielded brown dyes, which after initial sintering melted at 245, 254, and 232°, respectively.

Condensation between 3-mercaptophenanthrene and oxalyl chloride yields 1,2-phenanthro[3,4-*b*]thiophenequinone (II) (m.p. 239–240°) (702). II forms quinoxalines with *o*-phenylenediamine, 2,3-diaminoquinoxaline, and 2,3-diaminophenazine melting at 287, >290, and >290°, respectively.

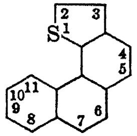
The only other derivative of this series is the 1-hydroxy-4-isopropyl-8-methyl derivative (III), which has been prepared from 6-retenethiol (285) (eq. 39). III could not be prepared in the pure state. It was obtained as a yellow oil which was readily oxidized in the air to a reddish-black amorphous solid. III can be condensed with isatin and various aldehydes to form amorphous solids which function as dyes in hydrosulfite vats.



(III)

(39)

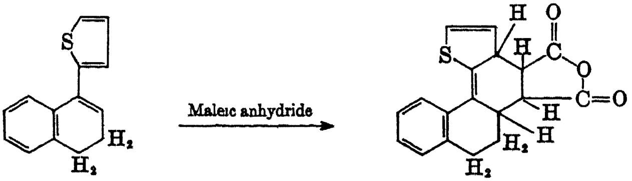
L. Phenanthro[4,3-*b*]thiophene



$C_{16}H_{10}S$

Phenanthro[4,3-*b*]thiophene (m.p. 91.5–92°, picrate 170–171°) has been prepared by the decarboxylation of phenanthro[4,3-*b*]thiophene-4,5-dicarboxylic anhydride (IV) over barium hydroxide and copper bronze (537). The 9-methoxyl derivative was prepared similarly (m.p. 88.5–89°, picrate 138–138.5°).

The reaction of maleic anhydride with 1-(2′-thienyl)-3,4-dihydronaphthalene (I) yields the mono adduct, 3a,4,5,5a,6,7-hexahydrophenanthro[4,3-*b*]thiophene-4,5-dicarboxylic anhydride (II) (eq. 40). In the presence



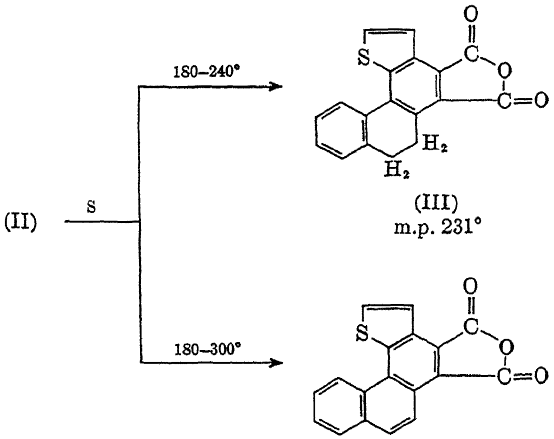
(I)

(II)
m.p. 212.9–213.4°
9-CH₃O derivative, m.p. 207.6–210.1°

(40)

of polar solvents, II and other similar adducts tend to dissociate and regenerate the diene. This was demonstrated by a study of the ultraviolet absorption spectra of these materials.

II can be completely dehydrogenated with sulfur to the aromatic material (IV) or to the 6,7-dihydro derivative (III) (eq. 41). It was proposed

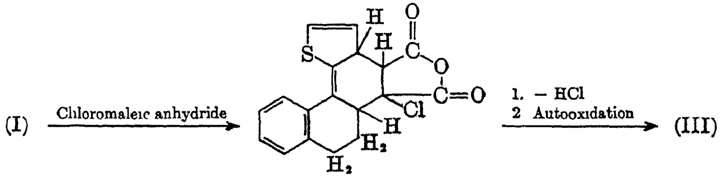


(III)
m.p. 231°

(IV)
m.p. 291.5–292.5°
$9\text{-}CH_3O$ derivative, m.p. 263.4–263.9°

(41)

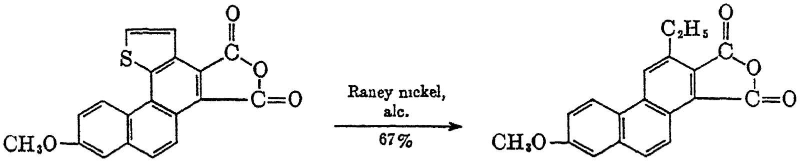
that II initially loses the two hydrogen atoms adjacent to the carbonyl group and is then autooxidized to III. Evidence in support of this theory was obtained by an independent synthesis of III (eq. 42). I reacts with



(42)

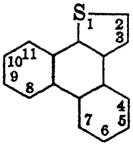
chloromaleic anhydride to form an adduct which loses a molecule of hydrogen chloride on sublimation. The unstable intermediate is autooxidized to the dihydro derivative (III). The chloromaleic anhydride adduct could not be obtained in the pure form.

The treatment of IV or its 9-methoxy derivative with Raney nickel and alcohol effects complete desulfurization and a degradation to the phenanthrene nucleus (538) (eq. 43). The yield with the unsubstituted material was 88%.



(43)

M. Phenanthro[9,10-*b*]thiophene

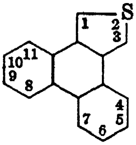


$C_{16}H_{10}S$

3-Hydroxyphenanthro[9,10-*b*]thiophene (I) m.p. 173–175°, has been made by the cyclization of 9-phenanthrenethioglycolyl chloride (167). Oxidation of I with potassium ferricyanide gave the symmetrical thioindigo dyes. I has also been coupled with phenanthraquinone, acenaphthoquinone, and isatin to give the unsymmetrical dyes. These dyes vary in color from chocolate to deep red.

Treatment of 9-phenanthrenethiol with oxalyl chloride yields 2,3-phenanthro[9,10-*b*]thiophenequinone, m.p. 245° (164). This material reacts with *o*-phenylenediamines to form quinoxalines (165) and with condensed hydroxythiophene derivatives to form unsymmetrical thioindigo dyes (166).

N. Phenanthro[9,10-*c*]thiophene



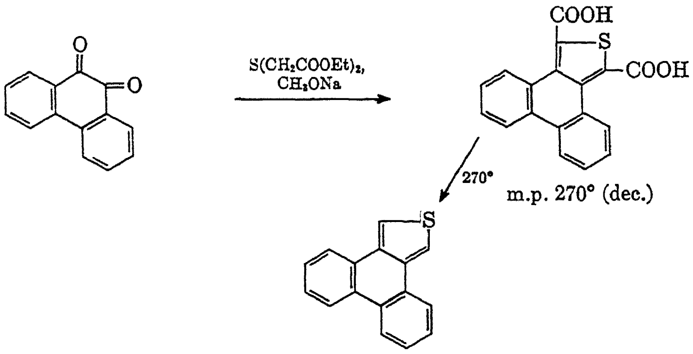
$C_{16}H_{10}S$

(*Ring Index* No. 2506)

Other Names

Phenanthroisothiophene
3,4-Diphenylenethiophene

Phenanthro[9,10-*c*]thiophene has been made by condensing 9,10-phenanthraquinone with ethyl thiodiglycolate followed by decarboxyla-



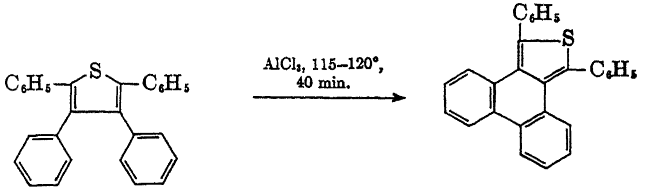
m.p. 270° (dec.)

m.p. 163°

(44)

tion (293) (eq. 44). The phenanthro[9,10-*c*]thiophene forms a yellowish-red color in sulfuric acid.

The heating of thionessal (tetraphenyl thiophene) (I) with aluminum chloride is claimed by Steinkopf to yield 1,3-diphenylphenanthro[9,10-*c*]-thiophene (II) in low yields (474) (eq. 45). However, from the reaction

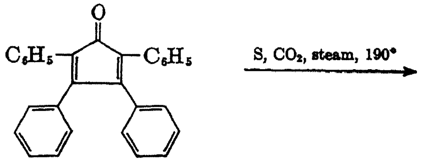


(I)

(II)
m.p. 260°

(45)

of phenylcyclone (III) with sulfur, which is known to form I initially, a product claimed to be II, but differing in properties from the material reported by Steinkopf, was isolated (146) (eq. 46). It is quite possible



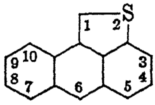
(III)

(II (?))
m.p. 204°

(46)

that these materials are different isomers, since the dehydrogenation of I could lead to a mixture of products, depending upon whether dehydrogenation occurred between the phenyl groups in the 3- and 4-positions or between those in the 2- and 3-positions. The latter dehydrogenation would lead to 2,3-diphenylphenanthro[9,10-*b*]thiophene.

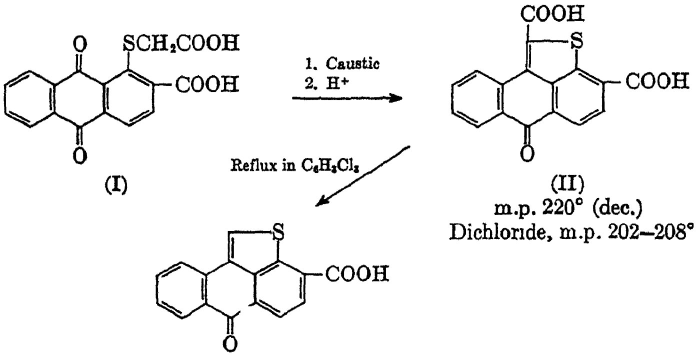
O. 6*H*-Anthra[1,9-*bc*]thiophene



$C_{15}H_{10}S$

(*Ring Index* No. 2507)

As was mentioned in the section on anthra[1,2-*b*]thiophene, ring closure of 2-carboxyanthraquinone-1-thioglycolic acid (I) in the presence of acetic anhydride occurs at either the 2- or 9-position or both, depending on the conditions used (P-438,P-435,P-208,P-433,P-259,P-436,P-622). Cyclization in an alkaline medium, however, takes place at only the 9-position to form the above ring system (P-434,P-448a,P-569,355,P-450) (eq. 47).



(I)

(II)
m.p. 220° (dec.)
Dichloride, m.p. 202–208°

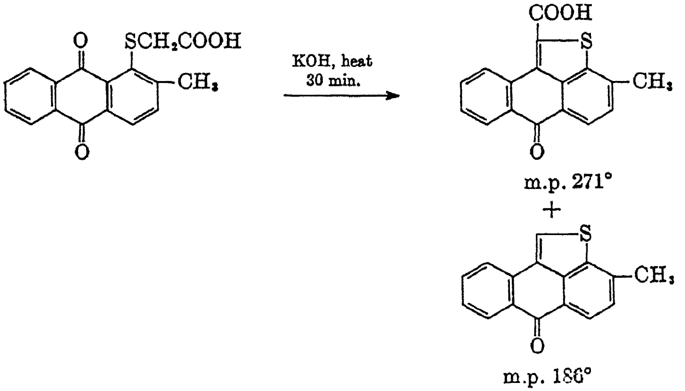
(47)

m.p.>300° Chloride, m.p. 256°

The acid chloride of III has been condensed with materials such as 1-aminoanthraquinone, 2-naphthylamine, etc. to form weak dyestuffs which color cotton yellow from a hyposulfite vat. Other brighter dyes have been obtained by the cyclization of sulfonic, amino, and acyl derivatives of I (P-484,P-592,P-594).

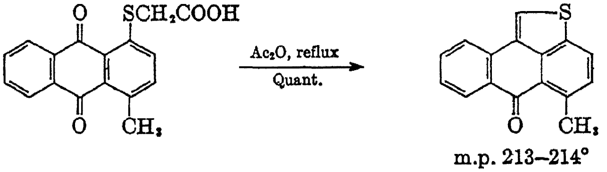
Cyclization of 2-methylanthraquinone-1-thioglycolic acid gives a mixture of the 1-carboxy and the corresponding decarboxylated material, 3-methyl-6*H*-anthra[1,9-*bc*]thiophene-6-one (227) (eq. 48). The methyl group of the latter material is easily oxidized to a carboxyl group by nitrobenzene in the presence of barium hydroxide or soda lime (P-209,P-113).

A quantitative yield of 5-methyl-6*H*-anthra[1,9-*bc*]thiophene-6-one

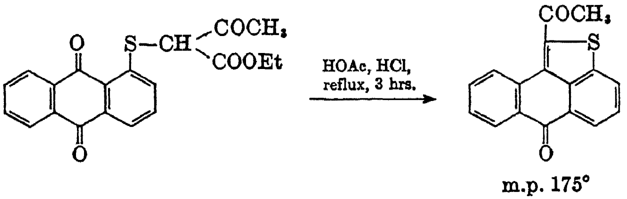


(48)

has been effected as shown in eq. 49 (574). It is surprising to find that these conditions are quite similar to those used to obtain the anthra[1,2-*b*]-isomer.



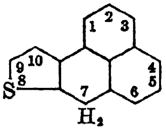
(49)



(50)

The 1-acetyl derivative has been made by the cyclization of eq. 50 (217). The 1-*p*-hydroxybenzoyl derivative was made in similar fashion. Attempts to prepare the 1-*o*-nitrobenzoyl derivative by this method were unsuccessful.

P. *7H*-Benzo[*ef*]thiophanthrene



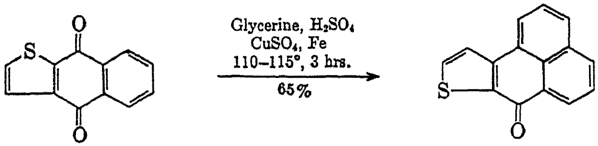
$C_{15}H_{10}S$

(*Ring Index* 2508)

Other Name

4 5 Benzothiophanthrene

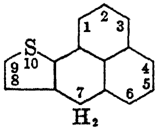
7*H*-Benzo[*ef*]thiophanthrene-7-one has been synthesized from thiophanthraquinone and glycerine (754) (eq. 51). This reaction was originally reported to yield the isomeric 7*H*-benzo[*jk*]thiophanthrene (P-608). However, subsequent work has shown that the oxidation of I yields an acid which is identical with the thiophanthraquinone-5-carboxylic acid obtained via the Sandmeyer reaction from 5-aminoanthraquinone.



(51)

(I)
m.p. 139–140°

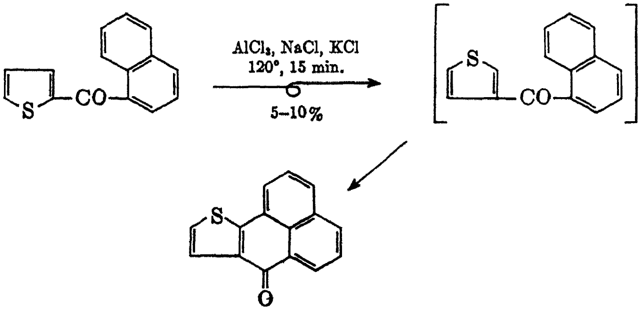
Q. 7*H*-Benzo[*jk*]thiophanthrene



$C_{15}H_{10}S$

Other Name
8,9-Benzothiophanthrene

The cyclization of 1-(2-thenoyl)naphthalene was first reported by Scholl and Seer (442) and later by Lee and Weinmayr (P-608) to yield the 4,5-benzothiophanthrone. Later work has shown that the condensation of thiophanthraquinone and glycerine yields the 4,5-isomer and that this material is different from that obtained by the cyclization of the thenoyl-



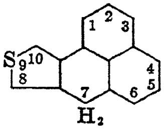
(52)

(I)
m.p. 215–217°, 250°

naphthalene (754). It has been presumed that rearrangement takes place during the cyclization and that the product obtained is the 8,9-isomer (eq. 52). In view of the many anomalous reactions occurring in this series, it would be desirable to substantiate the structure of I by oxidizing it to thiophanthraquinone-8-carboxylic acid and comparing it with the authentic 8-acid, which has been obtained from the amine via the Sandmeyer reaction.

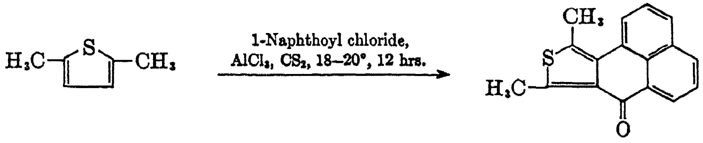
Widely different melting points have been reported for I (442,754). I gives a violet shade from a hydrosulfite vat and forms a reddish-brown color with concentrated sulfuric acid.

R. *7H*-Naphth[1,8-*ef*]isothianaphthene



$C_{15}H_{10}S$

It is claimed that this ring system results from the condensation of 2,5-dimethylthiophene and 1-naphthoyl chloride (81) (eq. 53). The 8,10-dimethyl 7*H*-naphth[1,8-*ef*]isothianaphthen-7-one forms a violet color with sulfuric acid.

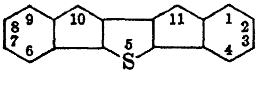


(53)

m.p. 165°

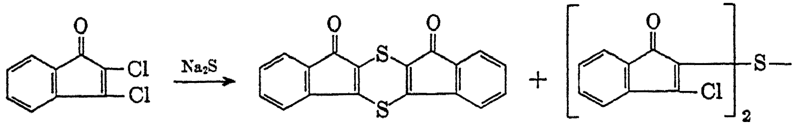
III. Five Ring Systems

A. Diindeno[1,2-*b*,2′,1′-*d*]thiophene



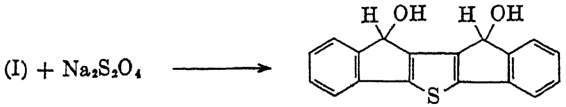
$C_{18}H_{10}S$
(*Ring Index* No. 2915)

The reaction of 2,3-dichloroindene-1-one with sodium sulfide is reported to yield compounds I and II (65) (eq. 54). Attempts to cyclize II with copper



(I) (II) (54)

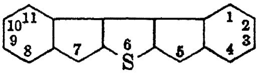
to a thiophene derivative were unsuccessful since desulfurization occurred. Alkaline reduction of I is accompanied by loss of sulfur and is claimed to yield III (eq. 55). III is soluble in sulfuric acid and forms a blue insoluble salt with sodium hydroxide.



(III)
m.p. 235–238° (55)

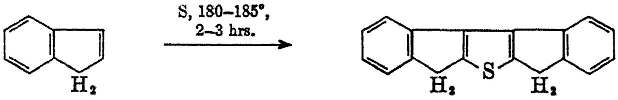
It should be pointed out that no proof of structure was given for III, and it seems quite possible that the sulfur may be attached to the 2-positions of the indene nucleus.

B. Diindeno[2,1-*b*,1′,2′-*d*]thiophene



$C_{18}H_{10}S$
(*Ring Index* No. 2916)

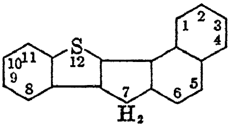
5,7-Dihydrodiindeo[2,1-*b*,1′,2′-*d*]thiophene is said to form from the reaction of sulfur and indene (214) (eq. 56). It forms a yellow-red adduct



m.p. 290–292° (56)

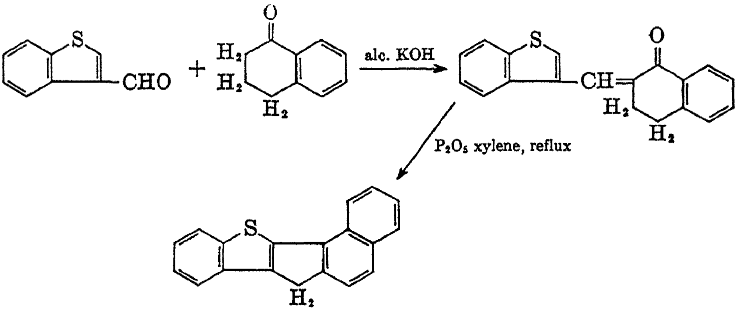
with tetranitromethane and reacts with nitric acid to form a dinitro derivative. No evidence other than analyses was presented to substantiate this structure.

C. 7*H*-Benz[6,7]indeno[1,2-*b*]thianaphthene



$C_{19}H_{12}S$

3-Thianaphthenecarboxaldehyde can be condensed with α-tetralone to form 2-(3′-thianaphthenal)-1-tetralone (90). The latter material undergoes an interesting intramolecular dehydration involving a complex shift of hydrogen (eq. 57).

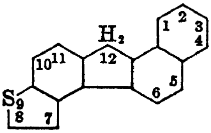


(57)

(I)
m.p. 147°
Picrate, m.p. 163°
Trinitrobenzene complex, m.p. 174°

I does not form a color in sufuric acid, but does show a blue-violet fluorescence in benzene. A comparison of the ultraviolet absorption spectra of I and its isolog, 13*H*-dibenzo[*a*,*g*]fluorene, was made and the patterns were found to be quite similar.

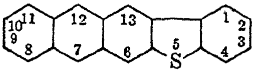
D. 12*H*-Benz[4,5]indeno[1,2-*e*]thianaphthene



$C_{19}H_{12}S$

12*H*-Benz[4,5]indeno[1,2-*e*]thianaphthene (m.p. 220°, picrate 179°) has been made from 1-naphthaldehyde and 4-oxo-4,5,6,7-tetrahydrothianaphthene by the method used for the synthesis of its isomer, 7*H*-benz[6,7]indeno[1,2-*b*]thianaphthene (637) (see eq. 57).

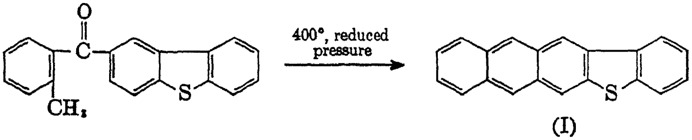
E. Dibenzo[*b*,*h*]thiophanthrene



$C_{20}H_{12}S$

(*Ring Index* No. 3128)

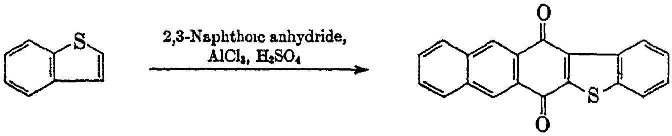
A French patent lists the preparation of dibenzo[*b*,*h*]thiophanthrene via the Elbs reaction (P-175) (eq. 58).



(58)

(I)
m.p. 249–250°

6,13-Dibenzo[*b*,*h*]thiophanthraquinone has been prepared from 2,3-naphthalenedicarboxylic anhydride and thianaphthene (378) (eq. 59).

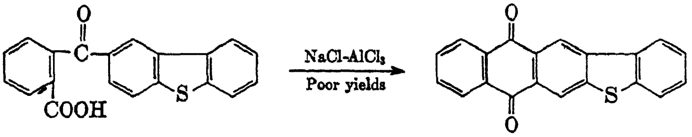


(59)

(II)
m.p. 301°

The 3-chloro-1-methyl derivative of II, m.p. 298–299°, has also been prepared by this method. The 7,12-dihydroxy derivative of II has been prepared by condensing 2,3-thianaphthenedicarboxylic anhydride and 1,4-dihydroxynaphthalene (P-421,P-93).

2-(2′-Carboxybenzoyl)dibenzothiophene can be cyclized to yield 7,12-dibenzo[*b*,*h*]thiophanthraquinone(III) (231) (eq. 60). A recent patent



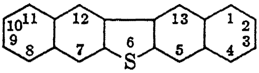
(60)

(III)
m.p. 285–286°

states that this ring closure can be effected in quantitative yields by heating in the presence of a mixture of orthophosphoric acid and phosphorus pentoxide (P-694). A number of substituted derivatives of III were also prepared by this method, but no melting points were listed.

Cyclization to form III can conceivably take place at either the 1- or 3-positions of the dibenzothiophene nucleus. However, from the work of Werner (526), which established that the ring closure of 4-(2'dibenzothienyl)butyric acid occurred at the 3-position, it seems plausible that the proposed linear structure is correct.

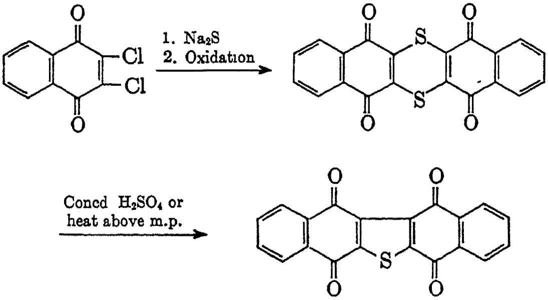
F. Dinaphtho[2,3,2',3']thiophene



$C_{20}H_{12}S$

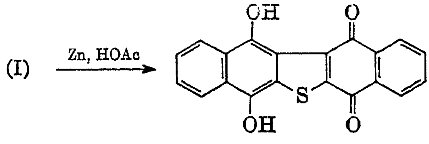
(*Ring Index* No. 3129)

The 5,7,12,13-tetraone derivative of dinaphtho[2,3,2',3']thiophene (I) has been synthesized from 2,3-dichloro-1,4-naphthoquinone by reactions



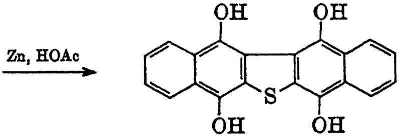
(I)
m.p. 278°

(61)



Blue monoacetate, m.p. 290°
Red diacetate, m.p. 254°

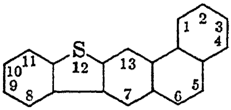
(62)



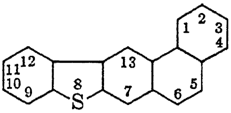
Yellow tetraacetate, m.p. 271° (dec.)
Yellow tetrabenzoate, m.p. 330° (dec.)

61 and 62 (64). Reduction of I yields both the di- and tetrahydroxy derivatives.

G. Dibenzo[*b*,*i*]thiophanthrene and Dibenzo[*b*,*g*]thiophanthrene



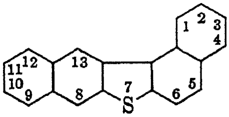
[*b*,*i*]
$C_{20}H_{12}S$
(*Ring Index* No. 3130)



[*b*,*g*]
$C_{20}H_{12}S$
(*Ring Index* No. 3131)

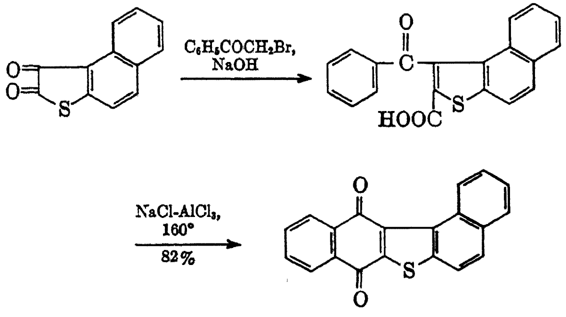
Materials believed to have the above basic ring systems were isolated from the reaction of thianaphthenedicarboxylic anhydride and naphthalene (378). The two isomeric 7,13-quinones, melting at 157 and 257°, respectively, were not further identified.

H. Dinaphtho[2,1,2′,3′]thiophene



$C_{20}H_{12}S$
(*Ring Index* No. 3132)

8,13-Dinaphtho[2,1,2′,3′]thiophenequinone has been synthesized from the reaction of 2,3-naphtho[2,1-*b*]thiophenequinone and phenacyl bromide followed by ring closure of the keto acid (378) (eq. 63).

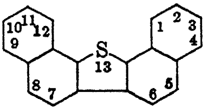


(63)

m.p. 252°

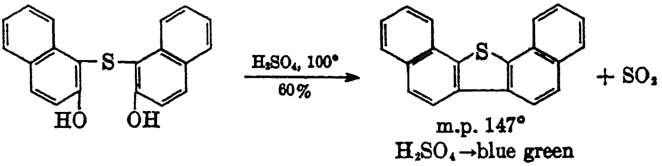
The manner in which phenacyl bromide and thianaphthenequinones react to form keto acids has been discussed previously.

I. Dinaphtho[1,2,2′,1′]thiophene



$C_{20}H_{12}S$

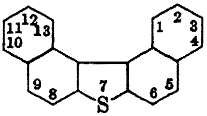
Dinaphtho[1,2,2′,1′]thiophene is claimed to have been prepared from bis(2-hydroxy-1-naphthyl) sulfide (287) (eq. 64). The mechanism of this reaction is not clear.



m.p. 147°
H_2SO_4 → blue green

(64)

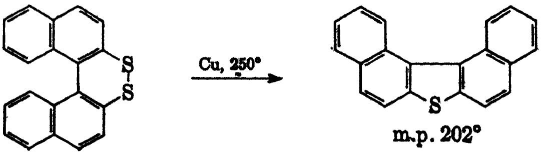
J. Dinaphtho[2,1,1′,2′]thiophene



$C_{20}H_{12}S$

(*Ring Index* No. 3133)

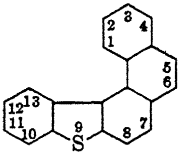
Dinaphtho[2,1,1′,2′]thiophene (I) has been made by the desulfurization of dinaphtho[2,1-*c*, 1′,2-*e*]-*o*-dithiin (30) (eq. 65). I is also claimed to be formed in extremely low yields from the action of sulfur on naphthalene in a tube heated to red heat (341). However, the reported melting point of this latter material is 250°.



m.p. 202°

(65)

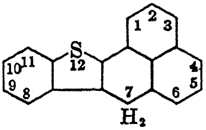
K. Phenanthro[3,4-*b*]thianaphthene



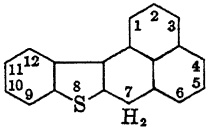
$C_{20}H_{12}S$

The 7,8-dicarboxylic anhydride of phenanthro[3,4-*b*]thianaphthene, m.p. 296–297°, has been prepared by the dehydrogenation of the adduct of maleic anhydride and 1-(3′-thianaphthenyl)-3,4-dihydronaphthalene (537). This reaction has been previously discussed (see eq. 1).

L. 7*H*-Dibenzo[*b*,*jk*]thiophanthrene and 7*H*-Dibenzo[*b*,*ef*]thiophanthrene

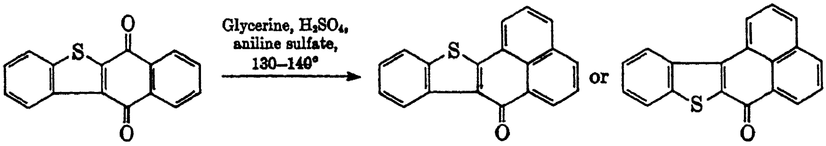


[*b*,*jk*]
$C_{19}H_{12}S$
(*Ring Index* No. 3134)



[*b*,*ef*]
$C_{19}H_{12}S$
(*Ring Index* No. 3135)

Several articles and patents describe the reaction of 6,11-benzo[*b*]-thiophanthraquinone and its derivatives with glycerine in the presence of sulfuric acid (378,P-540,P-43,P-68) (eq. 66). In all cases only one



(66)

(I) (II)
m.p. 172–173°, 182°

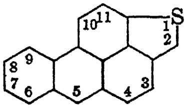
substance formed, which could be either I or II. No work on the structure of this material was reported. Subsequent studies carried out on thiophanthraquinone definitely established that cyclization involves only the oxygen furthest from the sulfur atom (754).* Therefore, it seems logical to assume that II represents the correct structure for the product formed from reaction 66.

---

* The position at which cyclization occurs was originally reported incorrectly (P-608).

Other derivatives of II prepared in identical fashion are the 4-methyl, m.p. 217–218°, 5-methyl, m.p. 183°, and 9-chloro-11-methyl derivatives, m.p. 305–306°. All of these materials are suitable dyes for cotton.

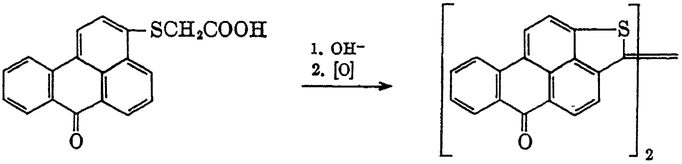
M. Anthra[2,1,9-*cde*]thianaphthene



$C_{18}H_{10}S$

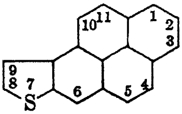
(*Ring Index* No. 3136)

A dye containing the above ring system has been synthesized according to eq. 67 (521,P-529,P-192). An acid is presumed to form during the alkaline cyclization which is decarboxylated during the mild oxidation step. Further experimental details were not given. This same dye is said to form from the fusion of 2-methyl-7*H*-benz [*de*] anthracene-7-one with sulfur or sodium polysulfide (P-681).



(67)

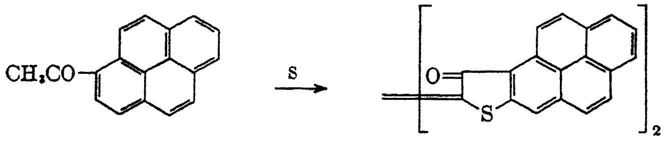
N. Pyreno[2,1-*b*]thiophene



$C_{18}H_{10}S$

(*Ring Index* No. 3137)

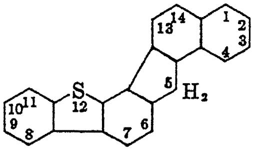
Fusion of 1-acetopyrene with sulfur yields a violet, brownish dye, m.p. >400°, which is believed to contain the pyreno[2,1-*b*]thiophene ring system (173) (eq. 68).



(68)

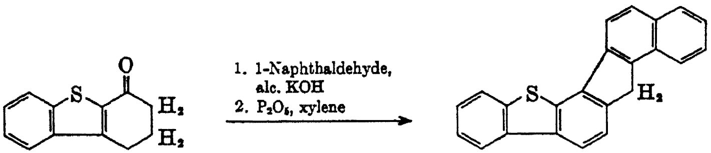
IV. Six Ring Systems

A. 5*H*-Naphth[1′,2′,2,3]indeno[4,5-*b*]thianaphthene



$C_{23}H_{13}S$

This material (I) has been prepared by the condensation of 4-oxo-1,2,3,4-tetrahydrodibenzothiophene with 1-naphthaldehyde (90) (eq. 69). I

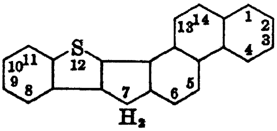


m.p. 204–205°
Picrate, m.p. 186°

(69)

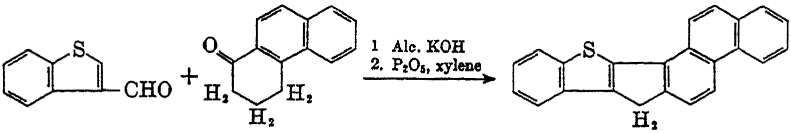
forms a picrate but unlike its isomer (see next section) does not form an addition compound with trinitrobenzene.

B. 7*H*-Naphth[1′,2′,6,7]indeno[1,2-*b*]thianaphthene



$C_{23}H_{13}S$

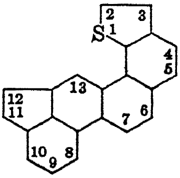
This material has been prepared from 3-thianaphthenealdehyde and -oxo-1,2,3,4-tetrahydrophenanthrene (90) (eq. 70).



(70)

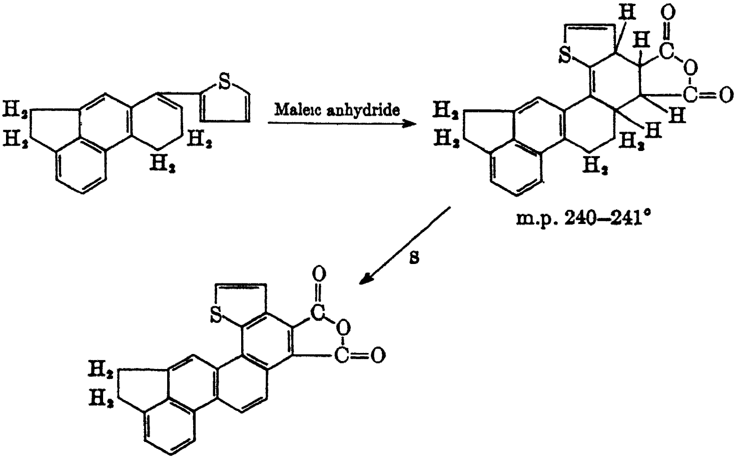
m.p. 227°
Picrate, m.p. 181°
Trinitrobenzene complex, m.p. 201°

C. Acephenanthryleno[7,8-*g*]thianaphthene



$C_{22}H_{12}S$

The above ring system has been made (eq. 71) by this previously dis-



m.p. 240–241°

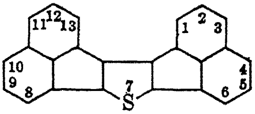
(71)

m.p. ca. 370°

cussed method (537) (see eq. 1). The aromatized anhydride was purified by sublimation at 280° (0.001 mm.).

V. Seven Ring Systems

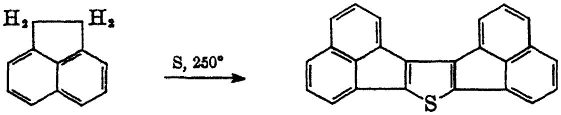
A. Diacenaphtho[1,2-*b*,1′,2′-*d*]thiophene



$C_{24}H_{12}S$

(*Ring Index* No. 3688)

Diacenaphtho[1,2-*b*,1′,2′-*d*]thiophene (I) has been prepared by a number of investigators by the fusion of sulfur with acenaphthene (168,103,112) (eq. 72). Fusion of the 5-benzoylacenaphthene with sulfur yields a dibenzoyl derivative of I, m.p. 213–215° (170).



(72)

(I)

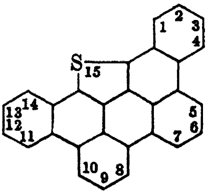
m.p. 278°, 276–278°, 285.5–286.5°

I reacts with bromine to form a material which can be oxidized to a bromonaphthalic acid (168). I also reacts with maleic anhydride to form an adduct which loses hydrogen sulfide on heating (112). The sulfonation of I leads to an extremely complex mixture of products (169). The nature of the products depends on the process. These mixtures are intensely colored and have the property of dyeing animal fibers.

The dipole moment of I has been found to be 0.8*D*, which is almost the same as the dipole moment found for dibenzothiophene (103).

VI. Eight Ring Systems

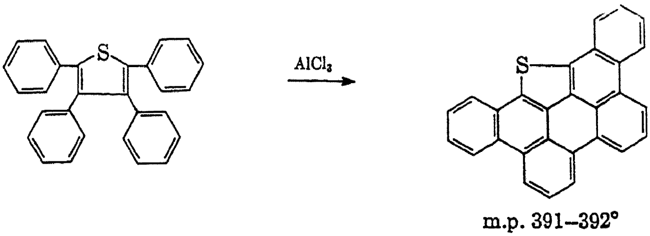
A. Flavophene



$C_{28}H_{14}S$

(*Ring Index* No. 3877)

The formation of flavophene is claimed to occur in very low yields from the reaction of tetraphenylthiophene (thionessal) and aluminum chloride (474).



(73)

1,3-Diphenylphenanthro[9,10-*c*]thiophene is also a product of this reaction (see eq. 45). Flavophene is orange yellow and imparts an olive green color to concentrated sulfuric acid. It forms a rust-brown hexanitro derivative with fuming nitric acid.

CHAPTER VII

Condensed Thiophene Compounds Containing O, S, and Hg Ring Systems

Introduction

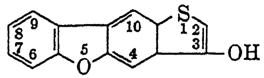
The assembly of this and the succeeding chapters has represented a difficult organizational problem. In order to maintain a logical sequence of discussion, it was necessary to depart from the numerical classification used by *Ring Index* and to arrange the systems according to the type of hetero ring system. Thus, all the hetero ring systems containing oxygen are discussed together irrespective of their *Ring Index* numbers.

The bulk of this chapter is concerned with the thienothiophenes. In most other cases, the parent ring systems have not been synthesized and the derivatives listed are formed by complex ring closures leaving residual functional groups attached to the parent ring system. In a great majority of the syntheses, it would not be feasible to consider preparation of the basic ring system by the methods listed.

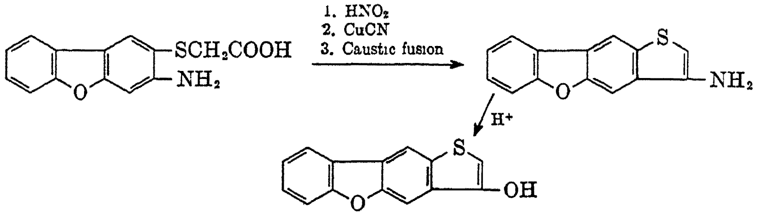
Substitution reactions have been carried out only with the thienothiophenes. The lack of preparative details, orientation studies, and precise physical properties of these compounds indicates that this is a most fruitful field for future investigators. One of the biggest contributions to this field would be a reinvestigation of the synthetic methods directed toward the synthesis of the parent compounds. Methods of substitution and determination of the position of substitution would also be extremely important to future development of these ring systems.

I. Furan Ring Systems

These ring systems are almost entirely composed of the anhydrides of dicarboxylic acids of thiophene and fused thiophene systems. Their preparation and properties are listed in the sections discussing their basic ring systems. Only the basic furan ring systems and their nomenclature are tabulated in this section. One furan ring system other than the anhydrides has been reported in the patent literature (P-467). This compound

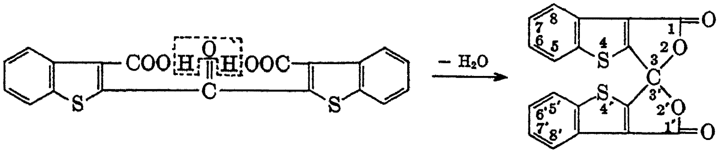


3-hydroxythianaphtheno[5,6-*b*]benzofuran, a C_4O-C_4S-C_6-C_6 system, is prepared by the sequence of reactions of eq. 1. The resultant compound gives brown to gray dyes when converted to asymmetrical thioindigo dyes.



(1)

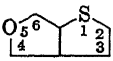
One spiro furan ring system, C_4O-C_4O-C_4S-C_4S-C_6-C_6, results from the dehydration of di-(3-carboxy-2-thianaphthenyl) ketone (378). This compound can be considered to be an internal dilactone of the parent compound (eq. 2). Compound I, 3,3′(1,1′(2*H*))-spirobi[furo[3,4-*b*]thianaphthene-1,1′-dione], *Ring Index* No. 3452, melts at 272–273°.



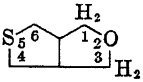
(I)

(2)

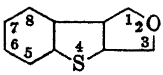
Following are nineteen furan ring systems which were obtained as anhydrides of the respective dicarboxylic acids of the corresponding lower ring systems. See parent ring systems for physical properties and references.



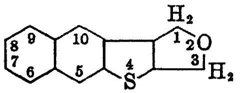
Ring Index No. 657
Thieno[2,3-c]furan



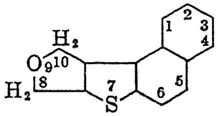
Ring Index No. 658
1,3(2*H*)-Thieno[3,4-*c*]furan



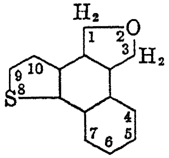
Ring Index No. 1436
Furo[3,4-*b*]thianaphthene



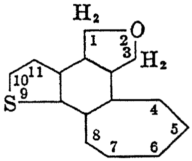
Ring Index No. 2303
1,3(2*H*)-Furo[3,4-*b*]thiophanthrene



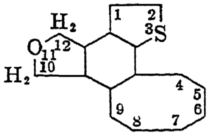
Ring Index No. 2304
8,10(2*H*)-Benzo[*e*]furo[3,4-*b*]thianaphthene



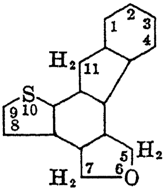
1,3(2*H*)-Benzo[*f*]furo[3,4-*d*]thianaphthene



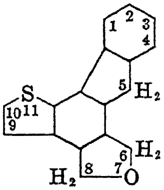
1,3,6-(3*H*)-Cyclohepta[*f*]furo[3,4-*d*]-thianaphthene



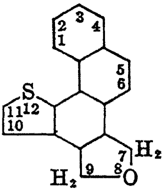
10,12(2*H*)-Cycloocta[*f*]furo[3,4-*d*]-thianaphthene



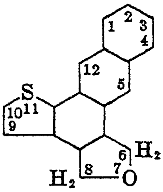
5,7,11(3*H*)-Furo[3,4-*d*]indeno[3,2-*f*] thianaphthene



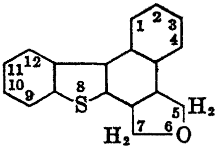
5,6,8(3*H*)-Furo[3,4-*d*]indeno[2,3-*f*]-thianaphthene



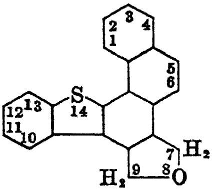
7,9(2*H*)-Furo[3,4-*d*]naphtho[2,1-*f*]-thianaphthene



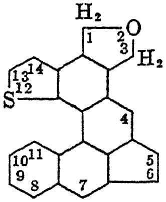
6,8(2*H*)-Furo[3,4-*d*]naphtho[2,3-*f*]-thianaphthene



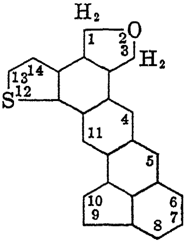
5,7(2*H*)-Dibenzo[*b*,*e*]furo[3,4-*g*]-thianaphthene



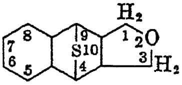
7,9(2*H*)-Benzo[*b*]furo[3,4-*e*]naphtho[2,1-*g*]-thianaphthene



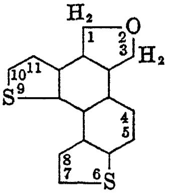
1,3(2*H*)-Furo[3,4-*d*]acephenanthryleno-[2,1-*f*]thianaphthene



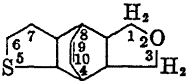
1,3(2*H*)-Aceanthryleno[8,9-*f*]furo[3,4-*d*]-thianaphthene



4,9-Thionaphtho[2,3-*c*]furan



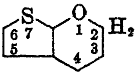
1,3(2*H*)-Furo[3,4-*d*]thianaphtheno[4,5-*f*]-thianaphthene



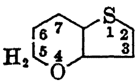
1,3(2*H*)-Furo[3,4-*e*]-4,8-endovinylene-thianaphthene

II. Pyran Ring Systems

A. The C_4S-C_5O Systems



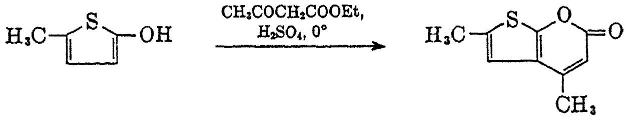
2*H*-Thieno[2,3-*b*]pyran



5*H*-Thieno[3,2-*b*]pyran

1. 2H-Thieno[2,3-b] pyran

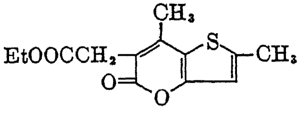
The parent compound of this series, as well as the isomeric ring system, is unknown. When ethyl acetoacetate is condensed with 2-hydroxy-5-methylthiophene, 2*H*-4,6-dimethylthieno[2,3-*b*]pyran-2-one results (382) (eq. 3). An attempt to convert a compound thought to be 2-hydroxy-thiophene to the corresponding pyrone failed.



(3)

2. 5H-Thieno[3,2-b]pyran

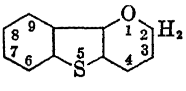
This system is obtained in the same manner as the isomeric system above by employing a substituted 3-hydroxythiophene. Thus, ethyl acetoacetate and 4-carbethoxy-3-hydroxy-5-methylthiophene yield 5*H*-2,7-dimethyl-3-carbethoxythieno[3,2-*b*]pyran-5-one (381), m.p. 14°. Under the same conditions, diethyl acetyl succinate forms ethyl 3-carbethoxy-2,7-dimethyl-5-oxo-5*H*-thieno[3,2-*b*]pyran-6-acetate (eq. 4). Citric acid produces the corresponding 3-carboxy-2-methyl-5-oxo-5*H*-thieno[3,2-*b*]pyran-7-acetic acid, m.p. 155°; ethyl acetylpropionate gives 3-carbethoxy-2,6,7-trimethyl-5*H*-thieno[3,2-*b*]pyran-5-one, m.p. 80°. Attempted condensations with ethyl oxalylacetate, ethyl formylacetate, or diethyl formylsuccinate did not give defined products.



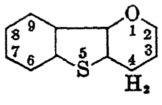
m.p. 107°

(4)

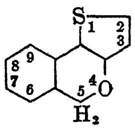
B. C_4S-C_5O-C_6 Systems



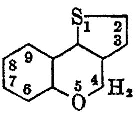
(*Ring Index* No. 1737)
2*H*-Pyrano[3,2-*b*]thianaphthene



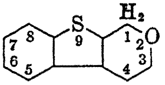
4*H*-Pyrano[3,2-*b*]thianaphthene



5*H*-Benzo[*d*]thieno[3,2-*b*]pyran



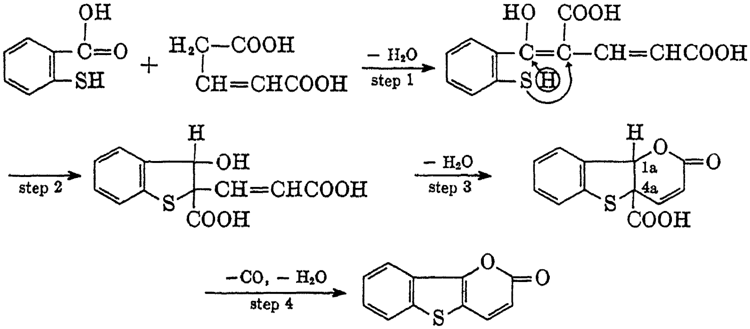
(*Ring Index* No. 1738)
4*H*-Benzo[*b*]thieno[2,3-*d*]pyran



1*H*-Pyrano[3,4-*b*]thianaphthene

1. 2H- and 4H-Pyrano[3,2-b]thianaphthenes

Synthesis of the 2*H* series is accomplished by condensation of unsaturated five or six carbon dibasic acids with 2-mercaptobenzoic acid in the presence of sulfuric acid at 25° (462). Thus, glutaconic acid is said to yield 2-oxo-2*H*-pyrano[3,2-*b*]thianaphthene (I) m.p. 176°. The reaction involves the elimination of three moles of water and one mole of carbon monoxide (eq. 5).



(5)

(I)

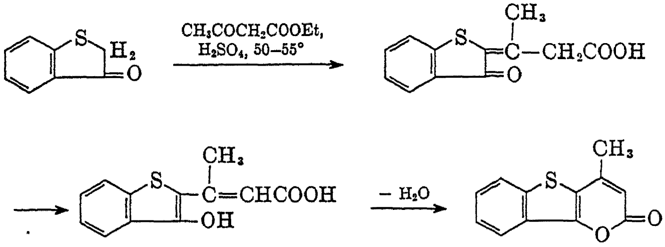
Steps 1, 2, and 3 are straightforward reactions involving (*1*) elimination of water between the carbonyl group and active methylene hydrogens, (*2*) the addition of the SH group to an adjacent vinyl group, and (*3*) the formation of a cyclic lactone similar to the reaction of coumarinic acid. In step 4, the elimination of carbon monoxide should produce a terminal hydrogen at the la or 4a positions, leaving a residual OH group at the other carbon that must be eliminated as water to yield the final product.

In a manner similar to that discussed above, chloroglutaconic acid yields the 4-chloro derivative of I, m.p. 173°. This material reacts with aniline to form the 4-anilino derivative, m.p. 281°. Impure dichloroglutaconic acid forms a mixture of the 4-chloro and 3,4-dichloro (m.p. 206°) derivatives of I. The latter when treated with aniline gives the 4-anilino-3-chloro derivative, m.p. 229°.

Treatment of 2-mercaptobenzoic acid with aconitic acid or hydroxymaleic acid in like manner gives 2*H*-2-oxopyrano[3,2-*b*]thianaphthene-4-

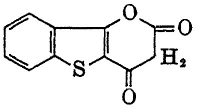
carboxylic acid, m.p. 285°. With alkaline reducing agents, this compound is said to yield "thioindigo." It is difficult to visualize how such a reaction could reduce this compound to either reactive forms of 2- or 3-hydroxythianaphthene if the structure is correctly represented by I.

Acetonylacetone condenses with 2-mercaptobenzoic acid at 50° in the presence of sulfuric acid to produce 4-methyl-2*H*-pyrano[3,2-*b*]thianaphthen-2-one, a pale buff crystalline compound, m.p. 164–165°. This compound also results in quantitative yield from the condensation of 3-hydroxythianaphthene with ethyl acetoacetate (460). Equation 6 may represent the course of the reaction.



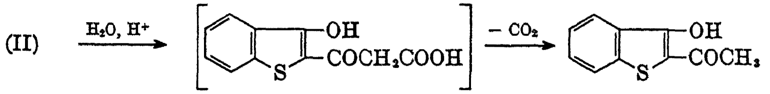
(6)

Acetonedicarboxylic acid or citric acid reacts with 2-mercaptobenzoic acid at 40–50° to produce 3,4-dihydro-2*H*-pyrano[3,2-*b*]thianaphthene-2,4-dione (461).



(II)
m.p. 275° (dec.)

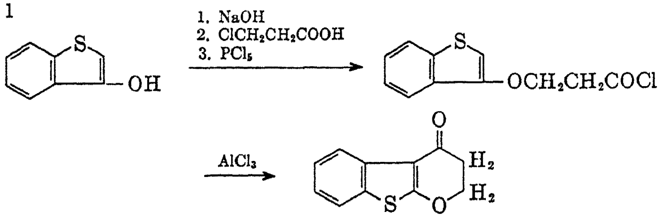
Compound II when treated with nitrous acid yields a yellow nitroso derivative. Formaldehyde (40%) in alcohol reacts to form a methylene bis derivative; the attachment is presumably through the 3-positions. Steam distillation in dilute acid converts II to 2-acetyl-3-hydroxythianaphthene (461). This reaction apparently substantiates the structure assigned (eq. 7).



(7)

The 4*H*-isomeric ring system of this series has been prepared by two methods (335).

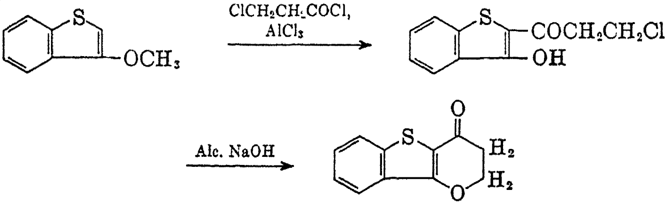
Method 1



(III)

(8)

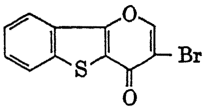
Method 2



(III)

(9)

Compound III, 2,3-dihydro-4-oxo-4*H*-pyrano[3,2-*b*]thianaphthene, b.p. 205° (12 mm.), m.p. 144–145°, forms a semicarbazone, m.p. 229–230°. With bromine in the absence of solvents, a compound said to be 3-bromo-4*H*-pyrano[3,2-*b*]thianaphthen-4-one (IV), m.p. 189–190°, is formed.

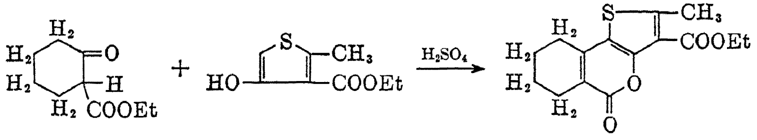


(IV)

Compound IV gave an orange color in concentrated sulfuric acid, but failed to react with dimethylaniline. When treated with sodium hydroxide it gave an acid, $C_{11}H_9O_3BrS$, m.p. 135–136°. Compound III does not react with benzaldehyde. In this respect, it differs in properties from the benzochromanones, which also brominated readily in the 3-position but which are not as susceptible to cleavage with caustic.

2. 5H-Benzo[d]thieno[3,2-b]pyran

This heterocyclic system arises from the condensation of a 3-hydroxythiophene and 2-carbethoxycyclohexanone (381) (eq. 10). Compound V, 3-carbethoxy-2-methyl-6,7,8,9-tetrahydro-5*H*-benzo[*d*]thieno[3,2-*b*]pyran-5-one melts at 175°; its free acid decomposes at 297°.

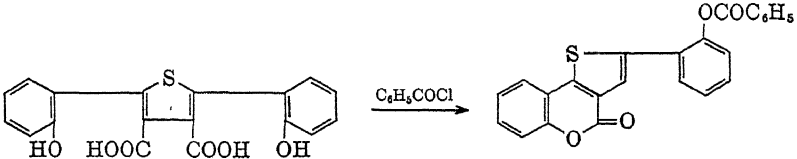


(V)

(10)

3. 4H-Benzo[b]thieno[2,3-d]pyran

Treatment of 2,5-bis(2′-hydroxyphenyl)thiophene-3,4-dicarboxylic acid with benzoyl chloride yields a small amount of a complex derivative of this system as well as the expected dibenzoxy compound (440) (eq. 11).

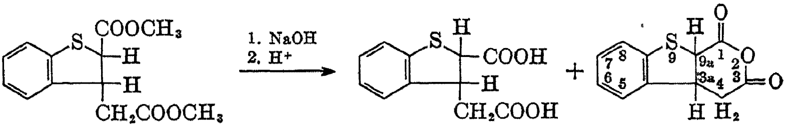


m.p. 211–212.5°

(11)

4. 1H-Pyrano[3,4-b]thianaphthene

The assignment of this ring system has been made by the present authors. The original investigators (620) obtained two products from the saponification and subsequent acidulation of the methyl ester of 2-carbomethoxy-2,3-dihydrothianaphene-3-acetic acid. While one product was assigned structure I, a second compound, $C_{11}H_8O_3S$, was obtained, and the original investigators suggested that it may have been an anhydride. If this compound is an anhydride it very likely contains the pyran ring system as shown by II (eq. 12). Compound II, 3,3a,4,9a-tetrahydro-1*H*-pyrano-[3,4-*b*]thianaphthene-1,3-dione, melts at 238–240°.

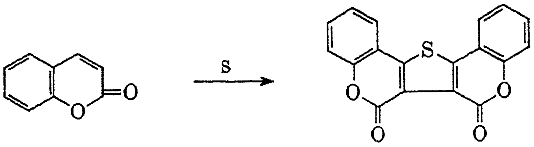


(I) (II)

(12)

C. C_4S-C_5O-C_5O-C_6-C_6 Systems

The only compound of this series is compound I, which is formed from the reaction of coumarin and sulfur at 220–230° (502,440) (eq. 13). The

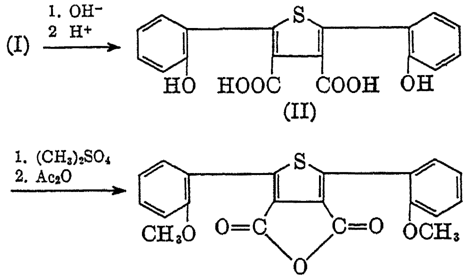


(I), m.p. 331–331.5°

(13)

parent ring system, *Ring Index* No. 3124, is thieno[3,2-*c*,4,5-*c*′] bis[*l*] benzopyran; compound I is the 6,7-dioxo derivative.

The structure of I was established by indirect evidence (440) (eq. 15).



(II)

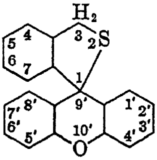
(III)

(15)

Although the structure of compound II was not proved by independent synthesis, the formation of the anhydride (III) seems to provide logical proof that the structure of I is correct. If the original point of attachment of the sulfur to the coumarin ring had been at the 3-position rather than at the 4-position, II would have been the isomeric 2,5-dicarboxylic acid which is not known to form a simple cyclic anhydride.

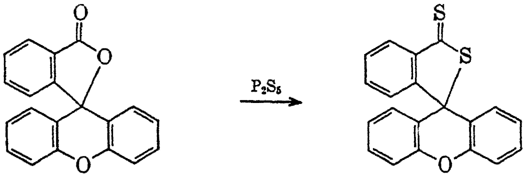
D. C_4S-C_5O-C_6-C_6-C_6 Systems

The only system of this series is spiro[isothianaphthene-1(3*H*),9′-xanthene], I, *Ring Index* No. 3125.



(I)

The 3-thioketo derivative of I (dithiafluoran) arises from the treatment of fluoran (II) with phosphorus pentasulfide (384) (eq. 16). The dichloro



(II) (III)

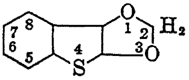
Brick red, m.p. 161–162°

(16)

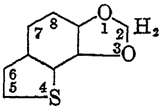
derivative of II yields a light red dichloro derivative of III, m.p. 196–197°. Adequate proof of the above ring system is not demonstrated in the original literature.

III. Miscellaneous O, and O,S Ring Systems

A. C_3O_2-C_4S-C_6 Systems



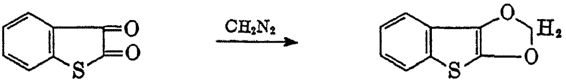
Thianaphtheno[2,3-*b*][1,3]dioxole



Thianaphtheno[6,7-*b*][1,3]dioxole

1. Thianaphtheno[2,3-b] [1,3]dioxole

The parent compound of this series is prepared by the action of diazomethane on 2,3-thianaphthenequinone (446) (eq. 17). Both acid hydrolysis and oxidation of compound I yield the original quinone.



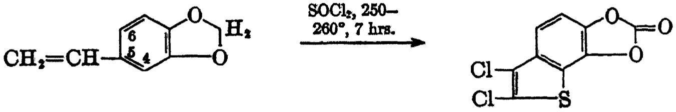
(I)

m.p. 130°

(17)

2. Thianaphtheno[6,7-b] [1,3]dioxole

When 5-vinylbenzo[*b*]dioxole or the 5-(1-hydroxyethyl) derivative is treated with thionyl chloride, a complex reaction takes place; it is reported that 5,6-dichlorothianaphtheno[6,7-*b*] [1,3]dioxol-2-one forms (32) (eq. 19).

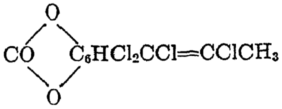


(II), m.p. 198°

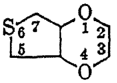
(19)

The original investigators pointed out that the ring closure could have taken place at carbon 6 instead of 4. In that case, the compound should be represented by the isomeric system, thianaphtheno[5,6-*b*] [1,3]dioxole.

Isosafrole dibromide, when treated with thionyl chloride, gives a very low yield of a compound thought to be 3,?-dichloro-2-methylthianaphtheno-[6,7-*b*] [1,3]dioxol-2-one (32), m.p. 180°. The principal product of the reaction was a compound having the empirical formula, $C_{10}H_4Cl_4O_3$, probably:



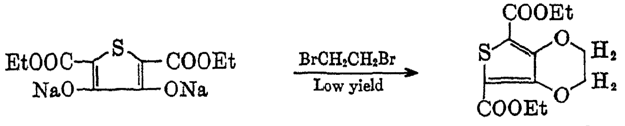
B. C_4S-C_4O_2 Systems



(*Ring Index* No. 847)

Thieno[3,4]-*p*-dioxin

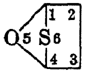
The parent compound of this series is unknown. The synthesis of 2,3-dihydro-5,7-dicarbethoxythieno[3,4]-*p*-dioxin is reported to occur in low yield when ethylene dibromide is reacted with the disodium salt of diethyl 3,4-dihydroxy-2,5-thiophenedicarboxylate (263) (eq. 20). This compound is reported to form a 5,7-di-*p*-sulfanilamido derivative when treated with *p*-sulfanilamide (306).



m.p. 275° (20)

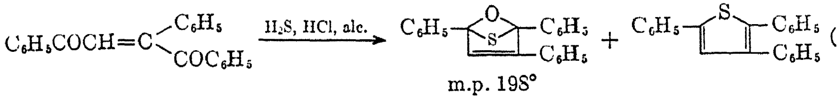
C. C_2OS-C_4S and C_2S_2-C_4S Systems

1. *5-Oxa-6-thiabicyclo[2.1.1]hexane*



(*Ring Index* No. 515)

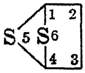
The only compound known in this series is 1,2,4-triphenyl-5-oxa-6-thiabicyclo[2.1.1]hexane, which has been prepared along with 2,3,5-tri-



(21)

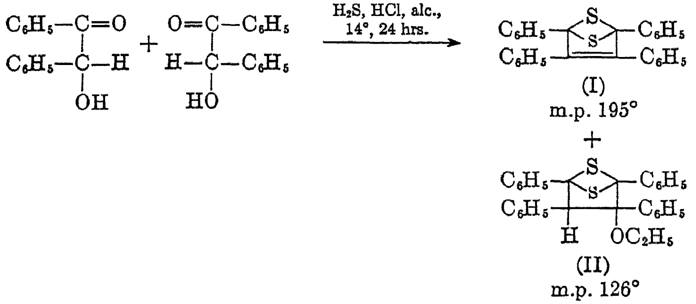
phenylthiophene by the method of eq. 21 (390). None of the reactions of this compound was investigated. Although no definite proof was presented for this particular structure, the assigned structure has some basis in fact, considering the reactions set forth in the following section.

2. 5,6-Dithiabicyclo[2.1.1]hexane



(*Ring Index* No. 519)

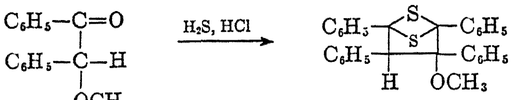
The parent compound of this series is unknown. Some of the complex phenyl derivatives are synthesized by a rather complicated condensation between benzoin and hydrogen sulfide (390) (eq. 22). In addition to com-



(22)

pounds I and II, a third compound of unknown structure (III) m.p. 97°, is formed. Compound II when treated further with hydrogen chloride yields compound I. Compound I is unaffected by zinc and hydrochloric acid and reacts slowly with potassium permanganate. Compound I takes up four atoms of bromine to form $C_{28}H_{20}Br_4S_2$. But, most significantly, it is converted to tetraphenylthiophene by the reduction action of hydriodic acid.

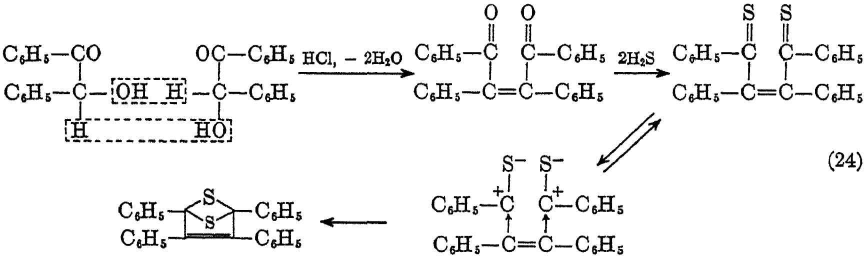
The methyl ether of benzoin reacts in a similar manner to form 2-methoxy-1,2,3,4-tetraphenyl-5,6-dithiabicyclo[2.1.1]hexane (390) (eq. 23). Compound IV, like Compound II, is converted to I on further treatment with hydrogen chloride.



(IV)
m.p. 195°

(23)

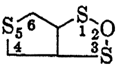
The structure of this class of compounds and the 5-oxa-6-thiabicyclo[2.1.1]hexanes above should be considered with some reserve until more adequate proof of structure is forthcoming. The best evidence presented is the conversion to tetraphenylthiophene by reductive removal of one sulfur atom. But this positive evidence is offset by the fact that the molecule adds four atoms of bromine. The latter reaction might indicate some open chain structure or the formation of a $>S{-}Br_2$ derivative. Since thioketones are known to dimerize or to trimerize and to yield thiophene-like compounds upon thermal degradation, the central 4-membered C_2S_2 ring in these compounds could be a simple internal dimer of the dithioketone. This could form as shown in eq. 24.



(I)

(24)

D. C_2OS_2-C_4S Systems

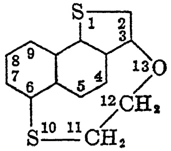


R.I. 587

Thieno [3,4-*c*] [1,2,5] oxadithiole

Known compounds of this series are internal anhydrides of 2,5-disubstituted-3,4-thiophenedisulfonic acids (344,472,473). These have been discussed in detail in *Thiophene and Its Derivatives*, page 420 (700).

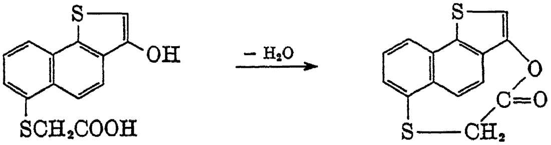
E. C_4S-C_6-C_6-C_8OS Systems



R.I. 2589

3,6-(Epoxyethanothio)naphtho[1,2-*b*]thiophene

The 12-oxo derivative of this system forms by lactonization of 3-hydroxynaphtho[1,2-*b*]thiophene-5-thioglycolic acid (116) (eq. 25). No



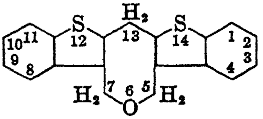
(25)

physical constants of this compound are reported. The C_8OS ring is quite unstable, as would be expected, and the compound is oxidized by air in caustic to the corresponding thioindigo dye of the naphtho[1,2-*b*]thiophene series.

F. Miscellaneous Macro Ring Systems

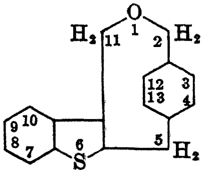
The two compounds which have been prepared are anhydrides of the respective dicarboxylic acids. Their physical constants and references are listed in Ch. II, Table II-21. Only basic ring systems are listed here.

C_4S-C_4S-C_6-C_6-C_7O:



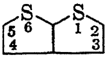
5,7,13(3*H*)-dithianaphtheno[3,2-*c*]oxepine

C_4S-C_6-C_6-C_9O:



IV. Multiple Thiophene Ring Systems

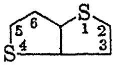
A. C_4S-C_4S Systems (Thiophthenes)



(I)

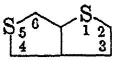
R.I. 664

Thieno[2,3-*b*]thiophene



(II)

Thieno[3,2-*b*]thiophene



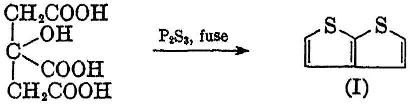
(III)

Thieno[3,4-*b*]thiophene

All three isomeric thienothiophenes are known; however, the [3,4-*b*] isomer is known only in the form of derivatives. Their chemistry appears to be quite similar to that of thiophene, *e.g.*, they may be acylated, halogenated, nitrated, and sulfonated readily when standard thiophene procedures are applied. In monosubstitution reactions of I and II, the 2-isomer is formed exclusively. A second substituent enters the nucleus at the 5-position.

1. Preparation and Identification of Thienothiophenes (I and II)

Soon after the synthesis of thiophene and its derivatives had been affected through the succinic acids or the β-diketo grouping of compounds such as acetonylacetone, Biedermann and Jacobsen (552) extended this synthesis to citric acid and tricarballylic acid, thus producing a compound, $C_6H_4S_2$, which was assigned the structure I and called thiophthene. The ring closure, as carried out with phosphorus trisulfide on citric acid and tricarballylic acid, gives less than 1% of thieno[2,3-*b*]thiophene (I) (eq. 26). In this manner, from 500 g. of citric acid and 1000 g. of phosphorus



(26)

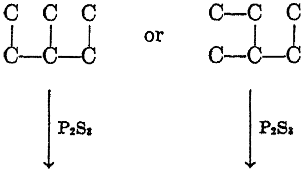
trisulfide, 3.3 g. of I was obtained by steam distillation of the oils which were formed from the reaction. The product was found to boil at 224–226° and to form a crystalline picrate (m.p. 133°). With bromine, a tetrabromo derivative (m.p. 172°) resulted. An adaptation of this synthesis by Hanna and Smith (553), using trisodium aconitate, gave thiophthene in yields similar to those from citric and tricarballylic acid.

Another synthesis giving somewhat better yields was developed almost simultaneously in 1908 by Capelle (554) and deConinck (555). It was observed in these instances that acetylene when passed through boiling sulfur vapors gave thiophthene as well as thiophene. R. Meyer and Wesche (385) studied the production of thiophthene from sulfur and acetylene. By their best technique, acetylene and hydrogen or methane when passed with hydrogen sulfide through a heated tube (640–670°) packed with Marquardt catalyst (FeS_2) gave thiophene, 2-methylthiophene, thianaphthene, and thiophthene. Later investigators (556,557) studied reaction variables and product distribution. The average composition of the liquid products formed from the reaction of acetylene and sulfur over the temperature range of 325–500° was 77% carbon disulfide, 9–12% thiophene, and 6% thiophthene. At 650°, the composition of the products was 83% carbon disulfide, 5% thiophene, and 3% thiophthene. In addition to the products reported above, later investigators (558) isolated thiophenol from the reaction products.

All of the earlier investigators failed to detect or separate the isomeric thiophthenes from the reaction mixtures, although some of them (385, 386,554) obtained tetrabromide derivatives melting at 172° and 229–230°. However, these were considered to be different crystalline forms of the tetrabromide of I. Their views were strengthened somewhat by the discovery that the picrate of I showed isomorphic properties with the picrates of both naphthalene and thianaphthene (386).

In 1935, Challenger, at the University of Leeds in England, became interested in thiophthene and began a study of its preparation and chemistry which is still active today. He and his coworkers chose to follow the method of Briscoe, Peel, and Robinson (556,557), but on a much larger scale. In making larger experiments two isomeric thiophthenes (I and II) were isolated and by tedius methods both could be obtained in a pure state. A detailed description of the apparatus, the procedure for carrying out the reaction, and the detailed purification procedure can be obtained from the article of Challenger and Harrison (559).

III has not been isolated from the reaction mixture. This is strange in view of the fact that all three isomeric selenophthenes are readily isolable from the reaction of selenium and acetylene. It should be pointed out, however, that Challenger and coworkers have only worked with the steam-volatile oils from this reaction and have isolated I and II from that source. In the selenophthene series one of the isomers was not volatile with steam (see Chapter IX). In the citric acid type of preparation (552,553) a considerable quantity of oil is obtained directly from the reaction mixture and only a small part of this is volatile with steam. The product has been shown to be I. If one examines the skeletal carbon system of these acids, it is seen that either I or III might conceivably form with equal ease in the following manner:



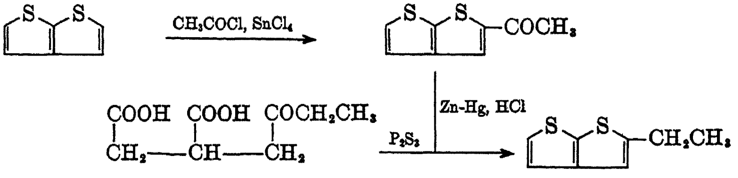
(I) (III)

Therefore, if III is not volatile with steam, it could have been neglected in the citric acid preparations and in the acetylene-sulfur procedure.

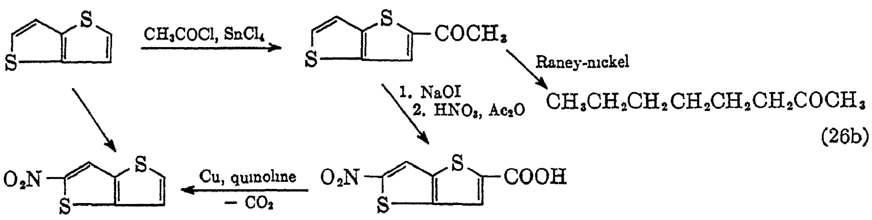
The structure of I has recently been established by means of an independent synthesis (757) which involves standard ring closure of 3-thiophenethioglycolic acid and reduction of the resultant thienothioindoxyl to thieno[3,2-*b*]thiophene by means of lithium aluminum hydride. The dipole moment, $\mu \times 10^{-18} = 1.16$ (measured on the product derived from acetylene) is also consistent with the structure given (559). The structure of II was established by means of its dipole moment (zero) (559).

2. Chemical Properties of the Thienothiophenes (I and II)

Monosubstitution reactions of both I and II occur at the 2-positions (757,715,559,560). No isomers are formed. The second substitution occurs at the 5-positions. The following sequence of reactions illustrates the methods used to establish orientation in these compounds (715,751) (eqs. 26a and 26b). In addition to the synthesis of 2-ethylthieno[2,3-*b*]thiophene (eq. 26a) the 3-ethyl isomer was synthesized from 1,2,3-pentanetricarboxylic acid and phosphorus trisulfide and was shown to be distinctly different from the 2-isomer obtained by the methods shown.



(26a)



(26b)

Prior to this recent work, Challenger and Gibson (560) had demonstrated that the acids obtained by oxidizing the acetyl derivative of II and by transmetalation of II with a Grignard reagent followed by carbonation were identical. Since this was the case with thiophene and dissimilar to the substitution of thianaphthene (3-substitution in the former case and 2-substitution with the Grignard), indirect evidence was provided for 2-substitution. It had also been shown that I, CH_3CO, MgBr, NO_2, and $HgOOCCH_3$ groups all enter the same position in II (715), later shown to be the 2-position (757).

Indirect evidence was also presented to show that the "liquid thiophthene" from the acetylene and sulfur reaction was properly represented by structure I rather than structure III (715). This was adduced by two observations: (*a*) that the nitration of the methyl ketone and the action of acetyl chloride and aluminum chloride on the nitrothiophthene yield identical nitro ketones and thence identical oximes; (*b*) that oxidation of the methyl ketone to the carboxylic acid, nitration, and decarboxylation yields the same nitro compound as is formed by direct nitration of I (715). In the case of III, if and when it is isolated, three isomeric substitution products might be expected, and the question of orientation in that molecule will be more complex.

The chemistry of the two known thiophthenes, I and II, appears to be quite similar to that of thiophene. All the techniques of substitution practiced thus far are standard for thiophene. II undergoes acylation readily, and yields as high as 88% of 2-propanoylthieno[3,2-*b*]thiophene result from treating II with propionyl chloride and stannic chloride in carbon disulfide solution (560). Acetic anhydride (II) and a trace of iodine give a 50% yield of methyl ketone derivative of II (715). II is mercurated normally, and the monomercurichloride of II can be reacted with acetyl chloride to give the acetylthiophthene (560), which is identical with the product obtained in 80% yield by direct acetylation of II (559). 2-Acetylthieno[2,3-*b*]thiophene is formed in 90% yield by the action of stannic chloride on I and acetyl chloride. The acetylthiophthenes can be reduced to the respective ethylthiophthenes by the Clemmensen method

(559). The ketones also form standard carbonyl derivatives such as the oximes, hydrazones, etc. and can be characterized in those forms (559,560).

2-Thiophthenecarboxylic acids are prepared by oxidation of the acetyl derivatives, by transmetalation of Grignard reagents (560), or by direct Grignard formation from the monoiodo derivatives of II (561) and I (562). The 2-iodo derivatives are prepared by the standard method involving iodine and mercuric oxide (561,562). Easily prepared derivatives for the identification of I and II are the tetrabromothiophthenes, obtained by exhaustive bromination in a solvent such as carbon disulfide or carbon tetrachloride (552,554,385,386,559,561). Bromination of II in cold, glacial acetic acid yields a dibromo derivative (561).

Isomers I and II give high yields of mononitro derivatives when nitrated by the acetyl nitrate technique (559,561). The 2-nitro derivative of II can be nitrated further with nitric acid (sp.gr. 1.52) to give a 2,5-dinitro derivative. Reduction of the mononitro derivatives by stannous chloride and hydrochloric acid gives the stannic chloride double salts of aminothiophthenes (559), which upon treatment with acetyl chloride yield the acetamido derivatives (559).

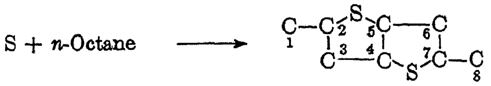
The reduction of II in sodium and alcohol yields 2-ethyl-3-thiophenethiol (559). Oxidation of thiophthenes with aqueous 4% potassium permanganate solution gave no sulfones. Complete degradation of the nucleus appeared to have taken place (559). Stannic chloride causes polymerization of thiophthene (561). Thieno[3,2-*b*]thiophene (II) is polymerized by orthophosphoric acid in glacial acetic acid to a yellow polymer that does not melt but sinters at 123–126° and blackens at 144° (561). Hydrogen bromide in the same solvent yields a pale-green polymer which darkens at 130° and decomposes at about 240°. The material appears to be dimeric (from molecular weight determinations) and contains a small amount of bromine (2%, much less than one equivalent per mole of thiophthene). Thieno[2,3-*b*]thiophene (I) and hydrogen bromide give a pale yellow product which deomposes above 150°. No molecular weight determinations were reported.

Both I and II cause poisoning of catalysts during batch hydrogenation of aromatic hydrocarbons, and a method of detoxification has been established by Maxted and Walker (376). The method consists of a preferential short hydrogenation period in which I and II are adsorbed on the catalyst surface and hydrogenated to products that are subsequently oxidized very readily by hydrogen peroxide or permolybdic acid. The products of the oxidation are not toxic to the catalyst. Hydrogenation of the aromatic hydrocarbon can then be carried out in a normal manner.

2-Acetylthieno[2,3-*b*]thiophene (from I) undergoes a typical Pfitzinger reaction and gives the corresponding, 2-(2-thieno[2,3-*b*]thienyl)cinchoninic acid, m.p. 262° (563). This compound is decarboxylated by standard techniques to give the 2-(2-thieno[2,3-*b*]thienyl)quinoline.

3. Friedmann's "Methyl- and Dimethylthiophthenes"

Friedmann (564,565) investigated the reactions of 2-octene and of octane with sulfur and found that the products consisted mainly of $C_8H_{12}S$ (IV) and $C_8H_8S_2$ (V). IV was thought to be a substituted thiophene, and although it failed to give an indophenine test with isatin and sulfuric acid it could be acylated in much the same manner as the alkylated thiophenes. V formed a dibromide, m.p. 170°, and Friedmann called it a "dimethylthiophthene" of the thieno[2,3-*b*]thiophene (I) series. This, however, could only arise from a deep-seated rearrangement of the C_8 structure. It was pointed out by Horton (300) that if compound V is a dimethylthiophthene it is more likely to be of type II rather than I, since dimethyl thieno[3,2-*b*]thiophene could be obtained in the following manner by ring closure by forming the sulfur bridges at carbons 2 and 5 and 4 and 7 without rearrangement of the carbon skeleton of the C_8 hydrocarbon (eq. 27).

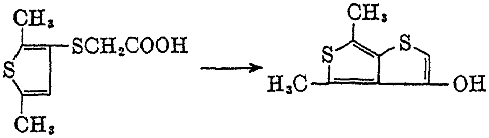


(27)

Later, Friedmann (566) in studying this reaction with *n*-heptane, postulated the same deep-seated rearrangement of the carbon skeleton to explain proposed structures of the observed products, $C_7H_{10}S$ (VI) and $C_7H_6S_2$, (VII). VII was reported to be a methylthiophthene of type I, but again it may be of type II, as shown in eq. 27 above. VI, which Friedmann (566) thought was an alkylthiophene, probably 3-isopropyl (?), could be further treated with sulfur to produce VII. However, he could not obtain such a compound by treating propylthiophenes with sulfur in the same manner, and admitted that the hydrogen analysis of VI was too high for the empirical formula given and may have represented alkylated thiolanes instead of thiophene. These, he presumed, would form VII if they were present. More recent studies of the action of sulfur on hydrocarbons by Farmer and Shipley (568) and Naylor (569,570) might indicate that VI contains the thiapyran ring system (C_5S) in some hydrogenated form. On the basis of this later work and the inability of Friedmann to convert the propylthiophene to VII, it is not entirely impossible that the "methylthiophthene" and "dimethylthiophthene" might contain a thiapyranthiophene ring system or two fused thiapyran rings. Therefore, in view of the lack of substantiating evidence, these compounds should not necessarily be classed as thiophthenes. Certainly, more precise chemical proof than that presented by Friedmann is essential for characterization.

4. *Synthesis of 3-Hydroxy-4,6-dimethylthieno[2,4-b]thiophene*

A private communication from Otto Dann in Germany describes the preparation of 3-hydroxy-4,6-dimethylthieno[3,4-b]thiophene by the thioglycolic acid synthesis employed in the thianaphthene series (eq. 27a). The



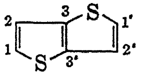
(27a)

compound is sensitive to air but it crystallizes in colorless needles when distilled, m.p. 115–118°. It was characterized as the orange 2-*p*-nitrobenzylidene derivative, m.p. 255° (dec.). The hydroxy compound is easily converted to a violet thienothioindigo dye. Above 300°, the dye turns black and decomposes without melting sharply.

5. *Physical Properties of Thienothiophenes*

Compounds I and II are volatile with steam and are separated in that manner from tarry reaction products in the preparations from citric acid and acetylene. However, it is rather difficult to separate them from each other and from the thianaphthene that occurs in small quantities from this reaction. Concerted attempts to purify the materials through several of their derivatives have not proved too satisfactory. Challenger and coworkers (559,560,561,562) were deeply concerned with this problem and found that the best method involved fractional crystallization of the styphnate or picrate salts (562). The phenomena of isomorphism (559, 386) appear to be more prevalent in this series than in the thiophene series, since the melting points of the picrates, styphnates, and the mononitro derivatives are not depressed upon mixing.

The physical constants of I and II and their derivatives are listed in Table VII-2. A fairly exhaustive study of the molecular structure of II has been carried out (130). It forms well-defined crystals from ligroin that are described as colorless bipyramids of the orthorhombic series. The form [111] is always present and generally predominates with occasionally [100], [010], or [001], but seldom more than one of them on any one crystal. X-ray study of the molecular structure indicated that the molecule exists in planar form. The investigators predict from the x-ray data that the compound has a structure which exists between two extremes, *i.e.*, the ground state with completely localized double bonds and the form which corresponds to complete delocalization of the π "unsaturation" electrons as in the molecule of benzene. Considering the molecule II (numbered for convenience by an unorthodox method), the bond orders and dimensions of the thieno[3,2-b]thiophene, as determined by x-ray studies (130), are collected in Table VII-1.



(II)

TABLE VII-1. Bond Orders

Bond	Theoretical		Experimental	
	Order	Length, A.	Order	Length, A.
C_1—C_2	1.76	1.37	1.85	1.36
C_2—C_3	1.56	1.41	1.58	1.41
C_3—C_3'	1.58	1.41	1.85	1.36
C_1—S	1.54	1.69	1.37	1.72
C_3'—S	1.49	1.70	1.27	1.74
Dimensions of the thieno[3,2-*b*]thiophene nucleus				
C_1—C_2	—	1.36	C_1—S—C_3'	91.2°
C_2—C_3	—	1.41	S—C_1—C_2	116.5°
C_3—C_3'	—	1.36	C_1—C_2—C_3	111.7°
C_1—S	—	1.72	C_2—C_3—C_3'	114.3°
C_3'—S	—	1.74	C_3—C_3'—S	110.2°
			C_2'—C_3'—S	135.5°

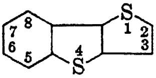
Other investigators (180), using a molecular-orbital method, which involves the *d* orbitals of the sulfur atom as developed by Longuet-Higgins for thiophene, calculated the bond orders and related them to bond lengths. The results are very similar to those listed here.

Both sets of investigators (130,180) commented on the difference between the calculated and experimentally determined lengths of the central C_3—C'_3 bond, but gave no explanation as to why it was shorter than expected. They did comment that this central bond discrepancy has also

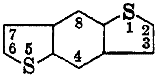
Deriv.	Thieno[2,3-*b*]thiophene, I		Thieno[3,2-*b*]thiophene, II	
	M.p., °C.	Ref.	M.p., °C.	Ref.
	6.25–6.50	552–559	56	559
	B.p. 224–226 (760 mm.)	385,386	B.p. 221–224 (760 mm.)	
	106 (16 mm.)	—		
Picrate	137–138	559,562	145	559,562
Styphnate	129.5–130.5	559,562	112–113	559,562
2-NO_2	125 5–126 5	559,715	124 5–125	559,715
2-$NHCOCH_3$	220.5–221.5	559,715	223.5 (dec.)	715
2,5-Dinitro	—	—	257–258	561
2-$COCH_3$	117	559,562	126–127	559,560
—, oxime	161	715	168	715
—, oxime acetate	105	715	120	715
—, oxime hydrochloride	169–172	715	175	715
—, *p*-nitrophenylhydrazone	241–242	559,562	246–247	559,560
—, 2,4-dinitrophenylhydrazone	267–268	559,562	267	559
2-COC_2H_5	—	—	92–92 5	560
Tetrabromo-	172	552,553,554,385,559	230–231	554,385,386,559
Tribromo-	123–123 5	559	Impure	559
2-Iodo	55.5	562	49	715
2,5-Diiodo-	—	—	190 5–191	561
2-HgCl	Above 280	559	Not detd.	559
2-COOH	245	562,715	219–220,223	560,715
—, methyl ester	106 5	562,715	96 5–97	560,715
—, *p*-nitrobenzyl ester	—	—	151–152	560
2,5-COOH	—	—	Above 300	560
2-$COCH_3$-5-NO_2	220	715		
2-C(=NOH)CH_3-5-NO_2	230 5	715		
2-COOH-5-NO_2	285 (dec.)	715		
2-$COOCH_3$-5-NO_2	164	715		

appeared in molecular-orbital calculations, which did not involve *d* orbitals, on molecules not containing hetero centers and that this discrepancy appears to be a more general feature than previously supposed. Longuet-Higgins (534), reviewing the data of Cox, Gillot, and Jeffrey (130), made calculations on this molecule assuming natural angles of 120° at $C'_2—C'_3—S$ and $C_2—C_3—S$ (Cox *et al.* determined this angle to be 135°). He concluded that the effect of strain in these angles acted to shorten the central bond $C_3—C'_3$ by about 0.06 A., which brings the calculated bond lengths into line with those determined experimentally by Cox *et al.* Schomaker (712) has also published comments on this general subject.

B. C_4S-C_4S-C_6 Systems

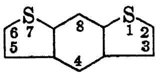


Thieno[3,2-*b*]thianaphthene



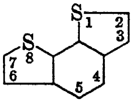
R I. 1444

Benzo[1,2-*b*,4,5-*b*′]dithiophene



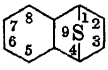
R.I. 1445

Benzo[1,2-*b*,5,4-*b*′]dithiophene



R.I. 1446

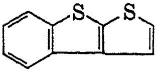
Benzo[2,1-*b*,3,4-*b*′]dithiophene



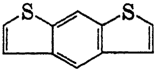
1,4-Thionaphthalen

1. *Lanfry's Reaction Product between Sulfur and Naphthalene (Thieno[3,2-b]thianaphthene?)*

Lanfry (340) obtained a product from a hot iron tube reaction of sulfur and naphthalene which melted at 118.5° and gave positive tests for thiophene with isatin (indophenine test) and phenanthraquinone (Liebermann test). Oxidation yielded a sulfone, $C_{10}H_6O_2S_2$, m.p. 130°, and a disulfone, $C_{10}H_6O_4S_2$, m.p. 125°. The compound formed a tetrabromide, m.p. 247–248°, and a tetranitro derivative which decomposed at 300°. From these considerations, Lanfry concluded that the original product, $C_{10}H_6S_2$, was either I or II.

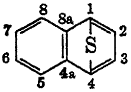


or



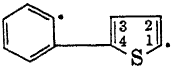
(I) (II)

It would not appear likely to the present writers that either I or II represents the correct formula, since the formation of either compound would require a most remarkable skeletal rearrangement of the carbon atoms. Herzfelder (289) previously found that 1-nitronaphthalene reacted with sulfur under less drastic conditions to give a compound $C_{10}H_6S$, to which the *endo* type formula III was assigned.



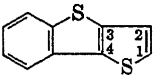
(III)

If such a compound is formed originally the second sulfur atom may attack to break the 1,8a or the 4,4a carbon bond to yield an intermediate (IV):



(IV)

which could conceivably react with sulfur to yield V without rearrangement of the carbon skeleton.

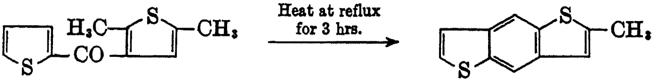


(V)

If the compound obtained by Lanfry actually contains the thiophene nucleus at all, thieno[3,2-*b*]thianaphthene (V) is considered to be a more likely formula than I or II.

2. Benzo[1,2-b,4,5-b′]dithiophene

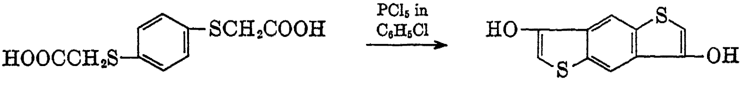
The parent compound of this series has not been reported. The 2-methyl homolog is said to form by thermal decomposition of 2,5-dimethyl-3-(2′-thenoyl)thiophene (85) (eq. 28). The investigators admitted that



(28)

their product, b.p. 189–190° at 13 mm., was of questionable structure as well as purity.

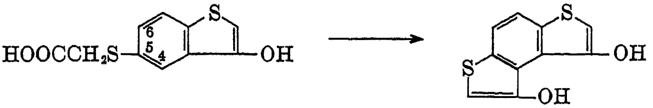
3,7-Dihydroxybenzo[1,2-*b*,4,5-*b*′]dithiophene has been prepared from *p*-phenyldithioglycolic acid (P-575) (eq. 29). The formula (VI) below



(VI)
m.p. 122–125°

(29)

represents the compound said to form in the original patent literature, but it should be pointed out that substitution reactions on the thianaphthene ring indicate considerable activity at the 4-position when the 5-position is substituted. Thus, if the intermediate (VII) were to close at the 4-carbon, a ring system isomeric with VI would form (eq. 30). Thus, either



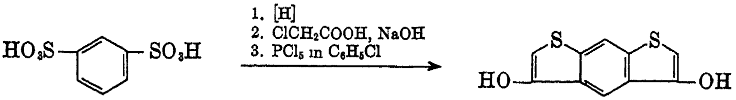
(VII) (VIII)

(30)

VI or VIII represents the structure of the product obtained. This material is reported to form typical thioindigo dyes.

3. Benzo[1,2-b,5,4-b′]dithiophene

3,5-Dihydroxybenzo[1,2-*b*,5,4-*b*′]dithiophene is the only compound of this series known. It is prepared as shown in equation 31 (P-575). Isomer



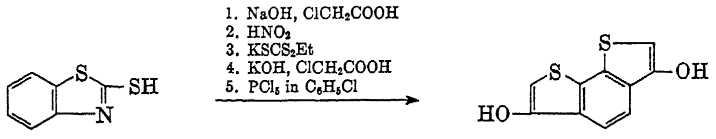
(IX), m.p. 108°

(31)

formation in this case is possible if the second ring closes at carbon 7 of the intermediate thianaphthene derivative. As in the case of its isomer, VI or VIII, compound IX is reported to form asymmetrical thioindigo dyes with suitable *o*-quinones.

4. Benzo[2,1-b,3,4-b′]dithiophene

The 3,6-dihydroxy derivative is the only example of this series of compounds. It is prepared from mercaptobenzothiazole by the following series



m.p. 157°

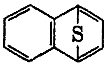
(32)

of reactions (P-575) (eq. 32). This compound undergoes typical reactions with *o*-quinones to produce thioindigo type dyes.

5. *1,4-Thionaphthalene*

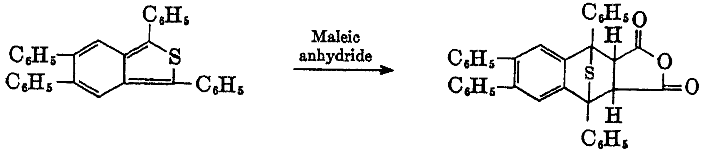
Actual proof that this ring system exists is lacking. From the evidence of Allen and Gates (3) discussed below, its existence appears more than probable and warrants some discussion.

Herzfelder (289) in 1895 reacted sulfur with 1-nitronaphthalene and obtained a dark-green amorphous powder, $C_{10}H_6S$, m.p. 155°, which he assumed from a study of properties to be compound I.



Evidence leading to assignment of the structure was (*1*) oxidation to phthalic acid, (*2*) addition of a limited amount of bromine to yield $C_{10}H_5BrS$, (*3*) bromination with excess bromine to yield 1,4-dibromonaphthalene, and (*4*) a molecular weight of 152 (158 calcd.). In addition, the compound could be sulfonated and nitrated (two nitro derivatives, m.p. 48° and 98–105°) without loss of the sulfur atom. Heating led to excessive decomposition.

Allen and Gates (3) have presented the best evidence for the existence of such a ring system and have also demonstrated the instability of the molecule. These investigators added maleic anhydride to a compound thought to be 1,3,5,6-tetraphenylbenzo[*c*]thiophene to obtain 1,4,6,7-tetraphenyl-1,4-thio-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic acid anhydride (eq. 33). This compound loses hydrogen sulfide in alcoholic

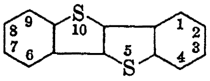


m.p. 245° (sec.)

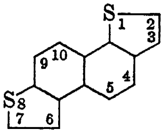
(33)

hydrogen chloride solution to form 1,4,6,7-tetraphenylnaphthalene-2,3-dicarboxylic acid. The only disturbing feature of this set of reactions is that other investigators (151) report that 1,3-diphenylbenzo[*c*]thiophene (see Chapter II, section B-II) failed to undergo a Diels-Alder synthesis with maleic anhydride, and it could be separated from its oxygen isostere (1,3-diphenylisobenzofuran) by this method.

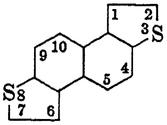
C. C_4S-C_4S-C_6-C_6 Systems



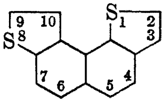
Thianaphtheno[3,2-*b*]thianaphthene



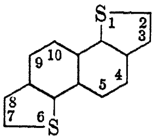
Thianaphtheno[4,5-*f*]thianaphthene



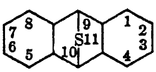
Thianaphtheno[5,4-*d*]thianaphthene



Thianaphtheno[5,4-*f*]thianaphthene

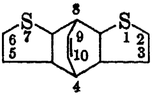


Thianaphtheno[7,6-*f*]thianaphthene



R.I. 2311

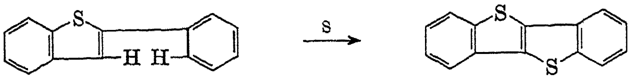
9,10-Thioanthracene



4,8-Endovinylenebenzo[1,2-*b*,5,4-*b*′]dithiophene

1. *Thianaphtheno[3,2-b]thianaphthene*

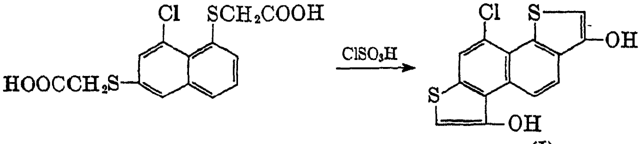
Horton (300) has shown that sulfur reacts with toluene to form tetraphenylthiophene and 2-phenylthianaphthene. On this basis he predicts that the compound $C_{14}H_{10}S_2$ (m.p. 209°) of Renard (606,607,610), obtained from the same reaction but at a higher temperature, is actually thianaphtheno[3,2-*b*]thianaphthene, $C_{10}H_8S_2$. If this is correct, then the second ring forms by "inter-ring" dehydrogenation (eq. 34). Renard indicated an


(34)

empirical formula of $C_{14}H_{10}S_2$, and called the compound a "phenyldithienyl." The structure was based on the positive indophenine and Liebermann tests for the thiophene ring. In addition, a dinitro derivative (m.p. 273°), a tribromo derivative (m.p. 320°), and a disulfonic acid derivative could be prepared from this compound. Even though the structure postulated by Horton cannot be accepted until more positive proof is presented, the "phenyldithienyl" structure hardly seems likely. It is indeed unfortunate that Horton (300) failed to carry out the above reaction on authentic 2-phenylthianaphthene to substantiate his postulation.

2. Thianaphtheno[4,5-f]thianaphthene

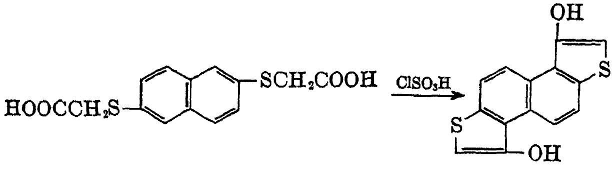
This system has been prepared in conjunction with thioindigo dyes. 5-Chloro-3,6-dihydroxythianaphtheno[4,5-*f*]thianaphthene (I) is formed in the usual manner by condensation of 4-chloro-2,5-naphthyldithioglycolic acid in the presence of chlorosulfonic acid (P-392) (eq. 35). Compound I was not isolated but was oxidized directly to a brownish-violet vat dye.


(I)

(35)

3. Thianaphtheno[5,4-d]thianaphthene

Until recently this system was known only as the 1,6-dihydroxy derivative which was prepared by the standard ring-closure method employing chlorosulfonic acid with 2,6-naphthyldithioglycolic acid (P-392) (eq. 36).

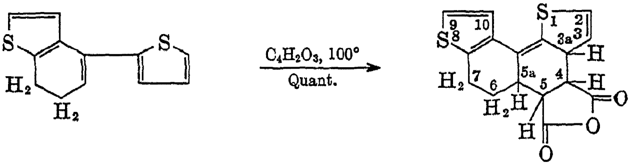

(36)

This compound was not isolated, but was oxidized directly to the corresponding thioindigo dye which, when vatted, tinted cotton in green shades.

The preparation of the parent compound has recently been announced by Tilak (764). When 1,5-bis(dimethoxyethylthio)naphthalene is heated with H_3PO_4-P_2O_5 for five minutes and then quickly poured onto ice, colorless thianaphtheno[4,5-*d*]thianaphthene, m.p. 263–265°, results. The compound forms an orange trinitrobenzene complex, m.p. 200–201°.

4. *Thianaphtheno[5,4-f]thianaphthene*

Like most isomers of this series, the parent compound is unknown. A partially hydrogenated derivative (II) is formed from the condensation of maleic anhydride and 4-thienyl 6,7-dihydrothianaphthene (537) (eq. 37). Similar systems having a single thiophene ring have been dehydrogenated with sulfur at 220–300° (see Chapter VI) to give the fully aromatic ring system, but this system was not so treated.

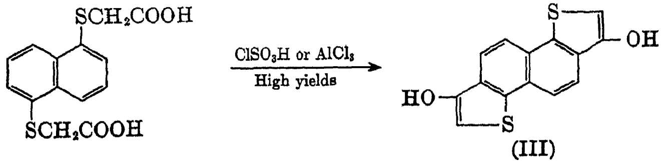


(37)

(II), m.p. 179–180°
3a,4,5,5a,6,7-Hexahydrothianaphtheno-[5,4-*f*]thianaphthene-4,5-dicarboxylic acid anhydride

5. *Thianaphtheno[7,6-f]thianaphthene*

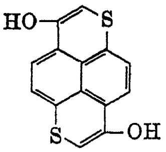
The 3,8-dihydroxy derivative (III) of this series is said to form by the ring closure of 1,5-naphthodithioglycolic acid (P-392,550). This product is normally not isolated, since it is converted almost entirely into the corresponding thioindigo dye by the reactants causing the original ring closure.



(III)

(38)

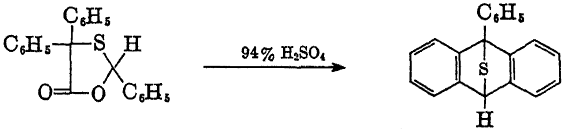
In addition, it is reported that a smaller amount of product, wherein the ring closure had taken place at the 4 and 8 carbons, was obtained (550). Thus, this slower reaction yielded the corresponding 1,6-dihydroxynaphtho[1,8-*bc*,5,4-*b'c'*]dithiapyran (IV).



This latter compound appears to have been obtained by most of the earlier investigators in this field, but it is difficult to ascertain whether or not their compounds contained the thiophene or thiapyran ring systems. Leandri (550) claims to have distinguished between the two forms, and states that ring closures take place more rapidly at the 2,6-carbons than at the 4,8-carbons, when aluminum chloride is used as the catalyst.

6. 9,10-Thioanthracene

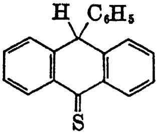
This series of compounds is said to arise from treatment of 2,4,4-triphenyl-1,3-oxathiol-5-one (I) with 94% sulfuric acid (88). The 9-phenyl-9,10-dihydro derivative is reported to form.



(II), m.p. 117–118° (39)

The 2-*p*-chlorophenyl-4,4-diphenyl derivative of I is reported to form the 2-chloro derivative of II, m.p. 124–126°.

The original investigators considered the alternate structure III for compound II. This was discarded when it was found that zinc and

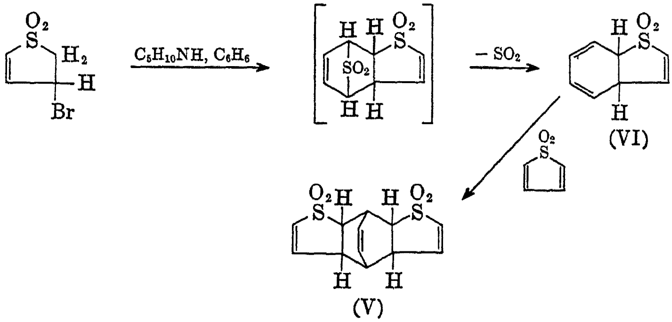


(III)

hydrochloric acid in acetic acid solution reduced the compound to a product thought to be 1,3-diphenyl-1,3-dihydrobenzo[*c*]thiophene (IV) which on further reduction yielded *o*-dibenzylbenzene. Oxidation of II with hydrogen peroxide in acetic acid yielded *o*-dibenzoylbenzene. *o*-Dibenzoylbenzene is also obtained by a similar oxidation of 9,10-diphenylanthracene (630).

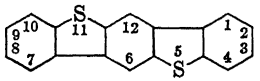
7. *4,8-Endovinylenebenzo[1,2-b,5,4-b′]dithiophene*

When 4-bromothiacyclopent-2-ene 1-dioxide is dehydrobrominated with piperidine in benzene, unstable thiophene 1-dioxide is formed. This undergoes an interesting internal Diels-Alder reaction, the end product of which is 3a,4,4a,7a,8,8a-hexahydro-4,8-endovinylenebenzo[1,2-*b*,5,4-*b*′]dithiophene 1,1,7,7-tetraoxide (V) (701) (eq. 39a). V decomposes without melting at 350°. Compound VI is isolable and can be shown to undergo the Diels-Alder reaction with maleic anhydride.



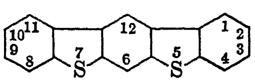
(39a)

D. C_4S-C_4S-C_6-C_6-C_6 Systems



R.I. 2989

Benzo[1,2-*b*,4,5-*b*′]bisthianaphthene

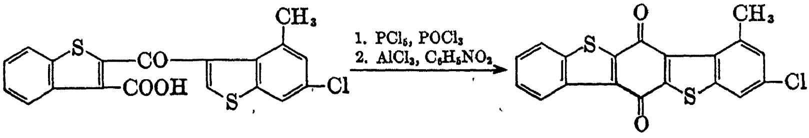


R.I. 2990

Benzo[1,2-*b*,5,4-*b*′]bisthianaphthene

1. *Benzo[1,2-b,4,5-b′]bisthianaphthene*

3-Chloro-1-methyl-6,12-dioxobenzo[1,2-*b*,4,5-*b*′]bisthianaphthene is the only compound of this series reported. The compound, a vat dye, is prepared in a typical anthraquinone-type ring closure (378) (eq. 40).

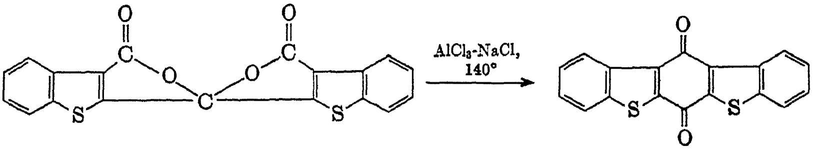


(40)

m.p. 260–262°

2. Benzo[1,2-b,5,4-b′]bisthianaphthene

The internal dilactone of 3,3′-dicarboxy-2,2′-thianaphthenyl ketone decarboxylates in the presence of aluminum chloride to yield 6,12-dioxobenzo[1,2-*b*,5,4-*b*′]bisthianaphthene (378,P-104,P-105,P-555) (eq. 41).



(41)

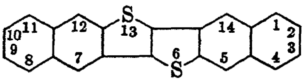
(I)

Dark red, m.p. 310–312°

This compound also results in 88% yield when 3-carboxy-2-thianaphthenyl-2′-thianaphthenyl ketone is treated stepwise with thionyl chloride and aluminum chloride. It is reported to give a cornflower blue color in sulfuric acid and to yield an orange vat.

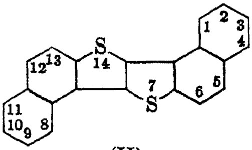
In a manner similar to that shown above, the brown 1-methyl-3-chloro derivative, m.p. 290°, the 3-ethoxy derivative, m.p. above 300°, and the red 1,11-dimethyl-3,9-dichloro derivative, m.p. 332°, of I have been prepared and characterized (378,P-104). The 3-hydroxy derivative, m.p. 220–230° (dec.), is obtained by hydrolysis of the 3-ethoxy derivative (378).

E. C_4S-C_4S-C_6-C_6-C_6-C_6 Systems



(I)

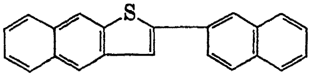
Naphtho[2,3-*b*′]thieno[2,3-*d*]naphtho[2,3-*b*]thiophene



(II)

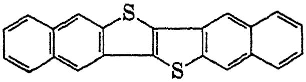
Naphtho[2,1-*b*′]thieno[2,3-*d*]naphtho[2,1-*b*]thiophene

Horton (300) makes the prediction from the work carried out with toluene and sulfur that the products obtained by Friedmann (611) from 2-methylnaphthalene are:



$C_{22}H_{14}S$

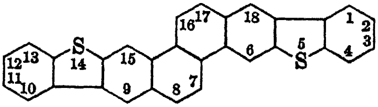
and



(I, $C_{22}H_{12}S_2$)
m.p. 350°

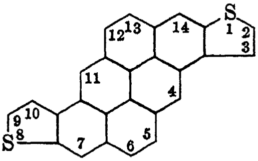
In such event, then the isomeric product obtained from 1-methylnaphthalene (611), m.p. 332°, may be compound II.

F. C_4S-C_4S-C_6-C_6-C_6-C_6-C_6-C_6 Systems



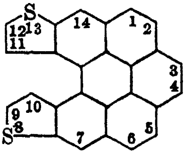
R.I. 3861

Chryseno[3,2-*b*,9,8-*b*′]bisthianaphthene



R.I. 3862

Pyreno[4,3-*ef*,9,8-*e*′*f*′]bisthianaphthene

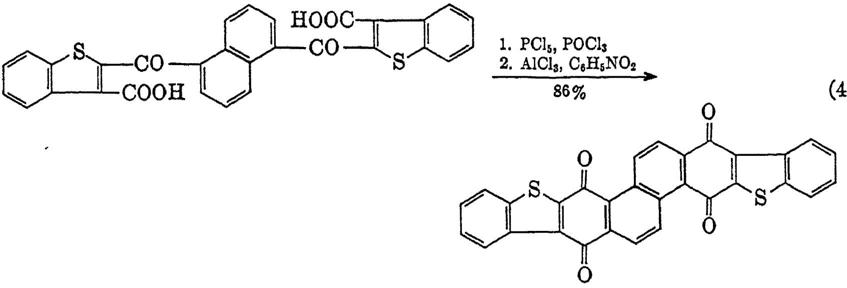


R.I. 3863

Pyreno[4,3-*ef*,5,6-*e*′*f*′]bisthianaphthene

1. *Chryseno[3,2-b,9,8-b′]bisthianaphthene*

Brown crystalline 6,9,15,18-tetraoxochryseno[3,2-*b*,9,8-*b*′]bisthianaphthene has been prepared by Mayer *et al.* (378) by the usual ring closure method employing 1,5-bis(3′-carboxythianaphthenyl)naphthyl diketone (eq. 42). The compound is reported to form an orange vat and to give a brownish-red color in sulfuric acid.

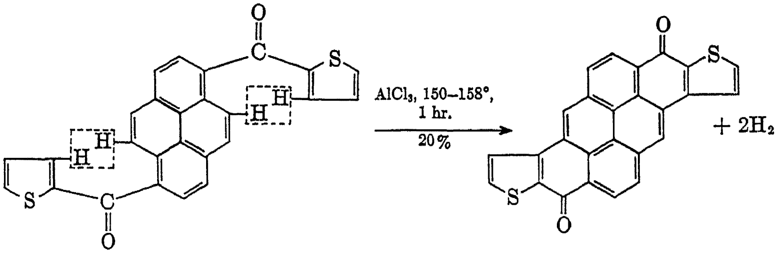


(42)

m.p. above 350°

2. *Pyreno[4,3-ef,9,8-e′f′]bisthianaphthene*

Reddish-brown 7,14-dioxopyreno[4,3-*ef*,9,8-*e′f′*]bisthianaphthene results from an aluminum chloride dehydrogenation reaction with 3,8-di(2′-thenoyl)pyrene (442) (eq. 43). While the melting point was not given,

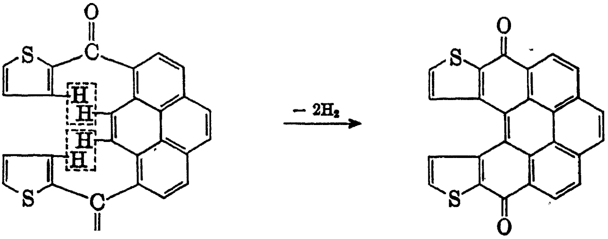


(43)

the investigators noted that the material gave a cherry-red hydrosulfite vat which showed deep-brown fluorescence.

3. *Pyreno[4,3-ef,5,6-e′f′]bisthianaphthene*

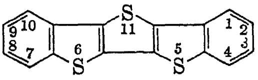
This system was prepared in the same manner as its isomer above from 3,10-di(2-thenoyl)pyrene. The resultant compound, 7,14-dioxopyreno-[4,3-*ef*,5,6-*e′f′*]bisthianaphthene, is brown and gives a bluish-violet vat (442) (eq. 44).



(44)

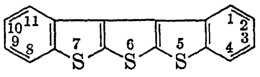
G. C_4S-C_4S-C_4S-C_6-C_6 Systems

Szperl (503) reacted thianaphthene with sulfur and obtained two colorless substances; one, $C_{16}H_8S_3$, m.p. 190–193°, and the second, a compound reported to be either a polymer or an isomer. On the basis of known reactions of sulfur with aromatic hydrocarbons such as indene, the structures of these two materials are probably represented by formulas I and II.



(I)

and

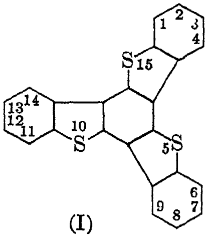


(II)

Thieno[3,2-*b*,2,3-*d*]bisthianaphthene (I)

Thieno[2,3-*b*,3,2-*d*]bisthianaphthene (II)

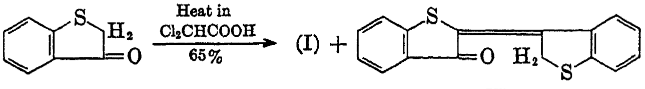
H. C_4S-C_4S-C_4S-C_6-C_6-C_6-C_6 Systems



(I)

Benzo[1,2-*b*,3,4-*b*′,5,6-*b*″]tristhianaphthene

A compound represented by formula I (m.p. 422–425°) is formed in 65% yield by refluxing 3-hydroxythianaphthene (keto form, II) in mono- or dichloroacetic acid solution. In addition, a product thought to be an intermediate, 2,3-dithioindoxyl (III) is formed (140*a*) (eq. 45). III is

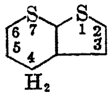


(II) (III) (45)

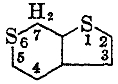
unchanged by boiling in chloroacetic acid, but addition of one mole of II yields I.

V. Thiapyran Ring Systems

A. C_4S-C_5S Systems



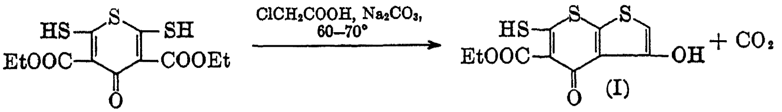
(*Ring Index* No. 852)
4*H*-Thieno[2,3-*b*]thiapyran



7*H*-Thieno[2,3-*c*]thiapyran

1. 4*H*-Thieno[2,3-*b*]thiapyran

Synthesis of this class of compounds is effected by reacting 2,6-dimercapto-3,5-dicarbethoxythiapyran-4-one with one mole of chloroacetic acid in alkaline solution (12). Ring closure takes place in this solution without isolation of the intermediate thioglycolic acid (eq. 46). Compound I is an orange-red crystalline material, m.p. 174.5°. A similar reaction employing chloroacetone yields the 2-acetyl derivative of I, an orange-yellow material, m.p. 143–144°. Phenacyl chloride yields the orange-red 2-benzoyl derivative of I, m.p. 175°. Compound I when treated with another mole of chloroacetic acid forms a second fused thiophene ring similar to the first ring. This is discussed under C_4S–C_4S-C_5S systems.

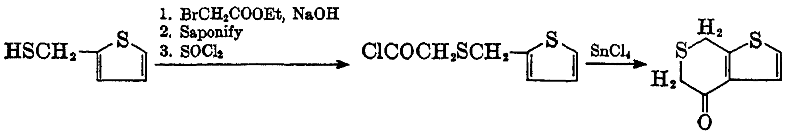


(46)

5-Carbethoxy-3-hydroxy-6-mercapto-4*H*-thieno[2,3-*b*]thiapyran-4-one

2. 7*H*-Thieno[2,3-*c*]thiapyran

The 4-keto derivative of this system results from the following sequence of reactions (545). Stannic chloride must be used for final ring closure, since aluminum chloride gives resinous products (eq. 47). Compound II

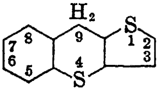


(47)

(II)
Oil, b.p. 167° (15 mm.)

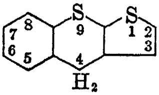
forms an oxime, m.p. 135°, and a semicarbazone, m.p. 288°. When ethyl 2-bromopropionate is employed in the original reaction instead of ethyl bromoacetate, the final product is 5-methyl-7*H*-thieno[2,3-*c*]thiapyran-4-one (III), b.p. 170° (16 mm.). The oxime of III melts at 151°; the semicarbazone melts at 259.5°.

B. C_4S-C_5S-C_6 Systems



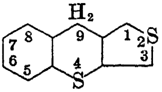
R.I. 1739

9*H*-Benzo[*b*]thieno[2,3-*e*]thiapyran



R.I. 1740

4*H*-Benzo[*b*]thieno[3,2-*e*]thiapyran

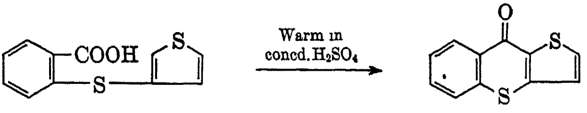


R.I. 1741

9*H*-Benzo[*b*]thieno[3,4-*e*]thiapyran

1. *9H-Benzo[b]thieno[2,3-e]thiapyran*

Steinkopf and Schmitt (480) prepared 9*H*-benzo[*b*]thieno[2,3-*e*]thiapyran-9-one by condensing 2-carboxyphenyl 3-thienyl sulfide (eq. 48).



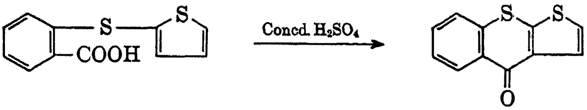
(I)

(48)

Compound I is a pale-yellow material melting at 161.5°. It gives a red solution in concentrated sulfuric acid.

2. *4H-Benzo[b]thieno[3,2-e]thiapyran*

4*H*-Benzo[*b*]thieno[3,2-*e*]thiapyran-4-one (II) has been prepared by the sulfuric acid ring-closure method from 2-carboxyphenyl 2-thienyl

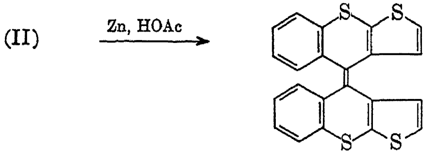


(II), m.p. 157–158°

(49)

sulfide (478) (eq. 49). Phosphorus pentachloride is also effective in this ring closure. In contrast to compound I, this isomer gives no color in concentrated sulfuric acid solution.

Reduction of II with zinc and acetic acid yields a 4,4′-dimer instead of the anticipated parent compound of this series (eq. 50).

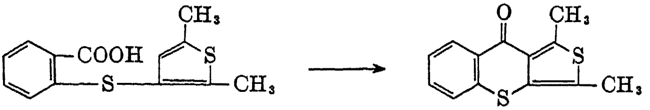


Yellow, m.p. 320–322°

(50)

3. 9H-Benzo[b]thieno[3,4-e]thiapyran

In a manner similar to that given in prior examples of this series, 9*H*-1,3-dimethylbenzo[*b*]thieno[3,4-*e*]thiapyran-9-one was prepared from the appropriate sulfide (482) (eq. 51). The ring closure is reported to take

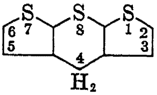


Yellow, m.p. 104–105°

(51)

place either with sulfuric acid or phosphorus pentachloride. This compound dissolves in concentrated sulfuric acid producing a deep red-violet solution.

C. C_4S-C_4S-C_5S Systems

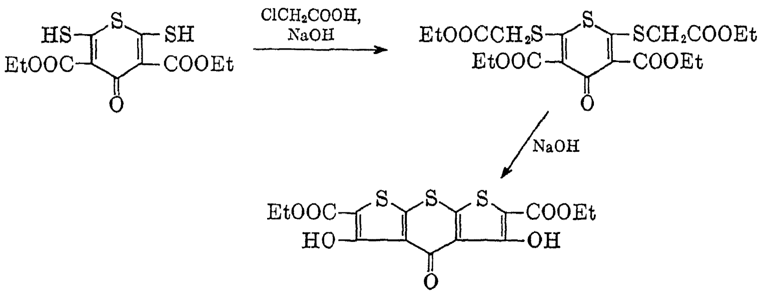


R.I. 1443

4*H*-Dithieno[2,3-*b*,3′,2′-*e*]thiapyran

This system was first prepared in 1908 by Apitzsch (11) by condensing 3,5-dicarbethoxy-2,6-dimercaptothiapyran-4-one with ethyl chloroacetate in alkaline solution (eq. 52).

Table VII-3 gives a series of derivatives of I which were prepared and characterized.



(52)

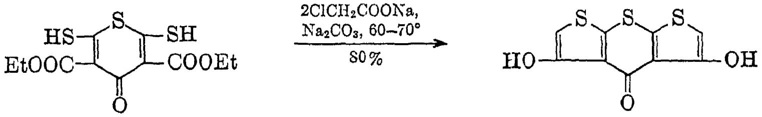
(I)

Bright yellow, m.p. 242°
2,6-Dicarbethoxy-3,5-dihydroxy-
4*H*-dithieno[2,3-*b*, 3',2'-*e*]-
thiapyran-4-one

TABLE VII-3

Substituents	M.p., °C.
2,6-Dicarbethoxy-3,5-diethoxy	216–217
2,6-Dicarbethoxy-3,5-dibenzoxy	263–267
2-Carbomethoxy-6-carbethoxy	245
2,6-Dicarbomethoxy-3,5-dihydroxy	294
2,6-Dicarbomethoxy-3,5-dibenzoxy	297–298
2,6-Dicarboamyloxy-3,5-dihydroxy	182
2,6-Dicarboamyloxy-3,5-dibenzoxy	202–203

If the reaction is carried out with sodium carbonate at 60–70°, decarboxylation results and yellow crystalline 3,5-dihydroxy-4*H*-dithieno[2,3-*b*-3',2'-*e*]thiapyran-4-one results (12) (eq. 53). The 3,5-diacetate derivative,

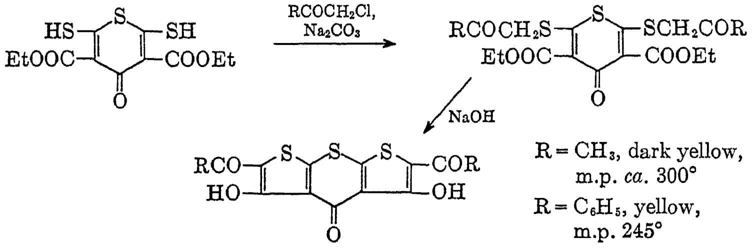


(53)

(II)
m p. 255° (dec.)

m.p. 174°, is colorless. Compound II is readily oxidized by air in alkaline solution to a thioindigo type dye. This dye is an amorphous black powder, but gives a brownish-red color in hydrochloric acid and yields a reddish-brown vat.

2,6-Diacyl derivatives are prepared by reaction with ClCH$_2$COR-type ketones in a step-wise condensation with sodium carbonate and sodium hydroxide (12) (eq. 54).



(III)

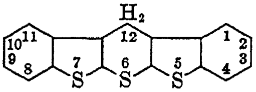
R = CH_3, dark yellow, m.p. *ca.* 300°

R = C_6H_5, yellow, m.p. 245°

(54)

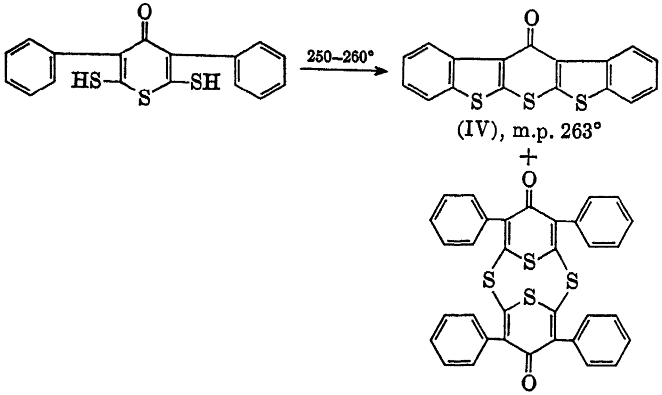
In compound III, where R is CH_3, three molecules of phenylhydrazine react to yield a trisphenylhydrazone, m.p. 261° (dec.).

D. C_4S-C_4S-C_5S-C_6-C_6 Systems



12*H*-Bisthianaphtheno[2,3-*b*,3′,2′-*e*]thiapyran

The 12-oxo derivative of this series results from the pyrolysis of 2,6-dimercapto-3,5-diphenyl-12H-thiapyran-4-one through loss of two molecules of hydrogen (448). A concurrent reaction in which hydrogen sulfide is eliminated yields a cyclic disulfide (V) (eq. 55). Compound IV is said

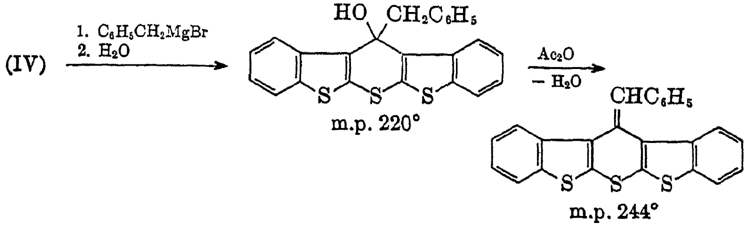


(IV), m.p. 263°

(V)

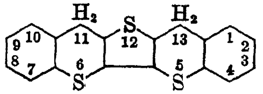
(55)

to add two molecules of RMgX to produce a R,R-disubstituted 12-derivative (449). Where R is $C_6H_5CH_2$, the 12,12-dibenzyl derivative melts at 176°; where R is C_6H_5, a compound of m.p. 235° is obtained; where R is *m*-tolyl, the 12,12-derivative melts at 219°. Addition of one mole of benzylmagnesium bromide yields a 12-benzyl-12-hydroxy derivative of IV, which can be subsequently dehydrated with acetic anhydride to yield the 12-benzylidene derivative (449) (eq. 56).



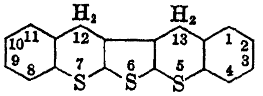
(56)

E. C_4S-C_5S-C_5S-C_6-C_6 Systems



R.I. 3126

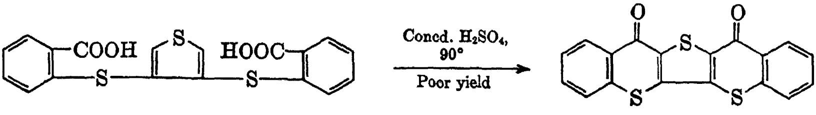
11,13(2*H*)-Thieno[3,2-*b*,4,5-*b*′]bis[1]benzothiapyran



12,13(2*H*)-Thieno[2,3-*b*,5,4-*b*′]bis[1]benzothiapyran

1. 11,13(2H)-Thieno[3,2-b,4,5-b′]bis[1]benzothiapyran

The 11,13-dioxo derivative of this series was prepared from 3,4-di(2-carboxyphenylthio)thiophene in a manner closely parallel to closure of the C_4S-C_5S-C_6 system above (478) (eq. 57). It was said in a later article that



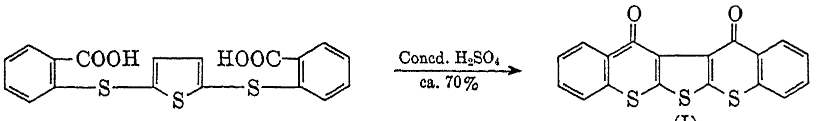
(57)

Yellow, m.p. 359–360°

this compound fails to form phenylhydrazones, although its isomer was able to form a bisphenylhydrazone (479).

2. 12,13(2H)-Thieno[2,3-b,5,4-b']bis[1]benzothiapyran

The 12,13-dioxo derivative of this series is said to form easily by an intramolecular dehydration reaction involving the two carboxy groups of 2,5-di(2-carboxyphenylthio)thiophene with the 3,4-hydrogens of the thiophene ring (478) (eq. 58). Compound I forms a monophenylhydrazone



(58)

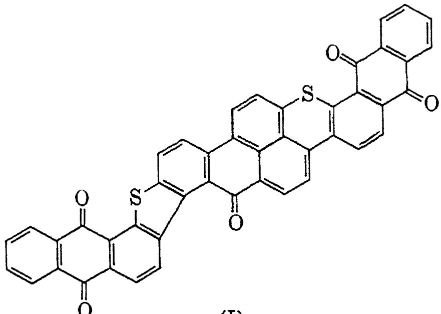
(I)
Yellow, m.p. 273°

(II) m.p. 222° (dec.), a picrate, m.p. 237–239°, and a green unstable pentabromide (478). With hydrazine hydrate it gives a low yield of a cyclic azine (see *Ring Index* system 3534, Chapter VIII, Section II-a-2). Compound II forms a deep blue perchlorate salt decomposing at 290–310°, a blue hydroxide salt that decomposes at 310–315°, and with iodine in benzene a greenish-black crystalline triiodide decomposing at 120–122°. I also forms a deep-blue benzylhydrazone whose purple perchlorate melts at 242–248° (dec.). Compound I was further noted to form citron-yellow amorphous addition complexes with acetyl chloride and thionyl chloride. With hydrogen chloride in chloroform, a yellow addition complex, I·2HCl, m.p. 273°, was obtained. By controlling the reactants, other yellow complexes of the formulas I·HCl, 3I·HCl, and 2I·3HCl are formed. Sulfuric acid forms a 1 : 1 addition complex. Apparently all of these complexes are unstable and lose water slowly upon standing.

Steinkopf points out that the chromophoric group in the hydrazones is not the typical quinoidal structure $[=N-NH=$ $=H_2]^+ X^-$, since the benzylhydrazones, which also form highly colored salts, are incapable of forming such a quinoid structure. Thus, he assumes the salt formation to occur at one of the thiapyran sulfurs forming a colored sulfonium type salt.

F. A C_4S-C_5S-$(C_6)_{10}$ System

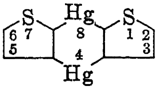
This ring system (I) is said to result from treatment of Bz-1_6-6-benzanthronyl di-1-anthroquinonyl disulfide with methanolic potassium hydroxide at 130–140° for several hours (P-601). The compound forms dichroic crystals from nitrobenzene and dyes cotton blue-gray from a blue-black vat.



(I)

VI. Mercury Ring Systems

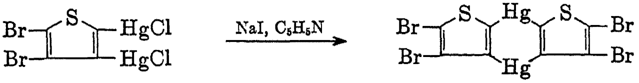
A. C_4S-C_4S-C_4Hg_2 Systems



R I. 1441

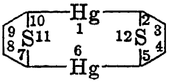
Dithieno[2,3-*b*,3′,2′-*e*]-*p*-dimercurin

This ring system is said to have been prepared as the 2,3,5,6-tetrabromo derivative from 4,5-dibromo-2,3-thiophenedimercurichloride (477) (eq. 59). The product is a brown amorphous solid. No melting point was listed in the original literature.



(59)

B. C_4S-C_4S-$C_4S_2Hg_2$ Systems

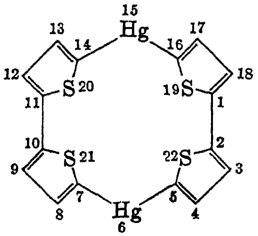


2,5,7,10-Dithiodimercurecin

This system is reported by Steinkopf and coworkers (477) to form from the reaction of pyridine and 2,5-thiophenedimercuriiodide at 30°. The product obtained in 35% yield is a gray powder that does not melt below 330°. 3-Ethyl-2,5-thiophenedimercurichloride yields a 3 (or 4), 8 (or 9)-

diethyl derivative, m.p. 310–315° (dec.). 3,4-Dimethyl-2,5-thiophenedimercurichloride yields the 3,4,8,9-tetramethyl derivative, m.p. 310° (dec.). The latter was obtained in 96% yield when NaI and pyridine were employed as the cyclizing agents. The 3,4,8,9-tetrabromo derivative (does not melt) was prepared in the same fashion.

C. C_4S-C_4S-C_4S-C_4S-$C_8S_4Hg_2$ Systems



R.I. 2896

Cyclic 5,5,5′,5′-dimercuribis-2,2′-dithienyl

This system is reported to form in 78% yield from the action of sodium iodide in pyridine on 5,5′-dimercurichloro-2,2′-dithienyl (475).

It should be pointed out in this case, as well as in the two preceding cases, that adequate evidence was not presented to substantiate this ring structure. Linear condensation could well have taken place, and the product in this case would probably have the structure—C_4H_2S—C_4H_2S—[Hg—C_4H_2S—C_4H_2S—Hg—C_4H_2S—C_4H_2S]$_n$Hg—.

CHAPTER VIII

Condensed Thiophene Compounds Containing Nitrogen Ring Systems

Introduction

As in Chapter VII, the objective of this chapter has been to summarize completely the condensed ring systems falling within this category. In order to conserve space, the various systems have been organized on the basis of common ring systems rather than on a ring progression system such as employed by *Ring Index*. Thus, the quinoxaline ring systems which were all made by the same synthesis could be tabulated, thereby saving considerable space.

More than a few of the following compounds containing these ring systems have been prepared only once, and, in many instances, only in quantities of a few milligrams. Many of the structures that have been represented are questionable, and, wherever possible, such discrepancies have been pointed out or corrected.

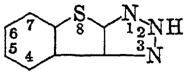
In general, the synthesis involved in preparing the nitrogenous ring systems employed standard techniques used in the benzenoid series, and are usually not unique to thiophene systems. Therefore, discussions of methods have been minimized.

No systematic study of the properties of these ring systems has been undertaken nor has any attempt been made to correlate the properties of these compounds with those of their benzenoid isologs. Some carbazole derivatives have been prepared by Buu-Hoï and coworkers in order to test their carcinogenic properties in relation to their benzenoid isosteres, but these data are not yet published. Thus, these systems offer an almost unexplored and seemingly fruitful field for a systematic study of properties, methods of synthesis, substitution reactions, and physiological activity.

I. Five-Membered Nitrogen Ring Systems

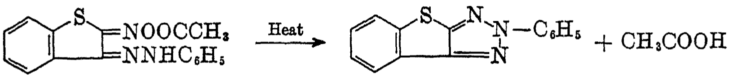
A. Triazole Ring Systems

1. C_2N_3-C_4S-C_6 *Systems*



(*Ring Index* No. 1326)
2*H*-Thianaphtheno[2,3]triazole

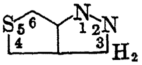
The 2-phenyl derivative of this system originates in a typical triazole ring closure by pyrolysis of the 2-(*O*-acetyloxime)-3-phenylhydrazone derivative of 2,3-thianaphthenequinone (19) (eq. 1). The resultant 2-phenylthianaphtheno[2,3]triazole is a colorless solid and fails to exhibit chromotropism in concentrated sulfuric acid.

 (1)

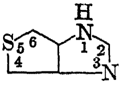
m.p. 152°

B. Diazole Ring Systems

1. C_3N_2-C_4S *Systems*



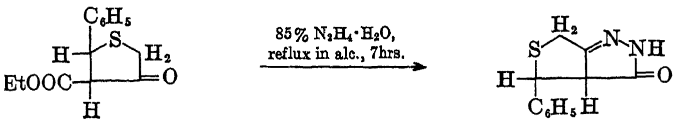
3*H*-Thieno[3,4-*c*]pyrazole



1*H*-Thieno[3,4-*b*]imidazole

(a) 3H-Thieno[3,4-c]pyrazole

The only compound of this series, 4-phenyl-3,3a,4,6-tetrahydro-3*H*-thieno[3,4-*c*]pyrazol-3-one, is formed by a conventional ring closure involving hydrazine and 2-phenyl-3-carbethoxythiacyclopentan-4-one (496) (eq. 2). None of the reactions of this compound was investigated.

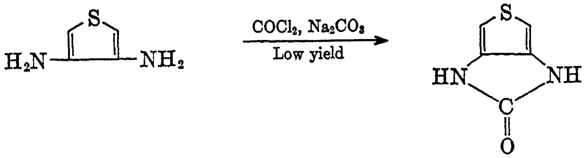
 (2)

m.p. 225–228° (dec.)

(b) 1*H*-Thieno[3,4-*b*]imidazole and Its Derivatives

This class of compounds consists of the aromatic analogs of the biotin series, the members of which are sometimes named as 2,3,4,5-tetradehydrobiotins (549). Aromatization of the thiophene ring in the dehydrobiotin nearly destroys the activity toward such organisms as *Lactobacillus arabinosus* and *Saccharomyces cerevisiae;* the aromatized material has less than one-four hundredth the activity of biotin. Due to the complexity and the diversity of the literature on biotin and its derivatives, no attempt to cover this system will be undertaken in this volume. For further literature, see the published work of Du Vigneaud, Baker, and Karrer from 1938 to the present and the summary of this subject by Blicke (617).

The compounds are generally prepared by ring closure of 3,4-diaminothiophene or its derivatives. In this manner, 1*H*-2,3-dihydrothieno[3,4-*b*]-imidazol-2-one was prepared by the action of phosgene on 3,4-diaminothiophene (548) (eq. 3).

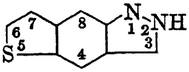


m.p. 200°

(3)

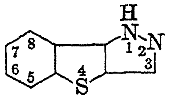
Cheney and Piening (104,549,P-667) have prepared the 4-γ-hydroxypropyl derivative (104), m.p. 139–140°, its phenyl ether, m.p. 174–175.5°, and its benzyl ether, m.p. 127–127.5° (P-667) and the 4- δ-valeric acid derivative, m.p. 253–254° (549, P-667). The latter compound appears in the literature under the name of 2′-keto-3,4-imidazolido-2-thiophenevaleric acid. This nomenclature is used predominantly in this series due to the circumstances of synthesis of the final compound by ring closure of thiophene derivatives.

2. C_3N_2-C_4S-C_6 Systems

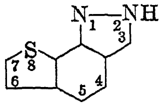


(*Ring Index* No. 1377)

2*H*-Thieno[2,3-*f*]indazole



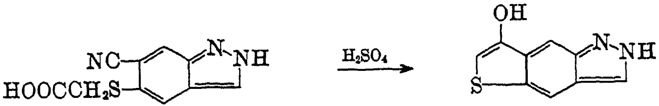
(*Ring Index* No. 1378)
1*H*-Thianaphtheno[3,2-*c*]pyrazole



(*Ring Index* No. 1379)
2*H*-Thieno[3,2-*g*]indazole

(a) **2*H*-Thieno[2,3-*f*]indazole**

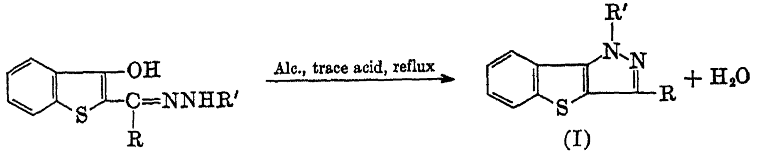
The 7-hydroxy derivative of this series has been prepared through the standard thioglycolic acid ring-closure method employing 6-cyano-5-indazolethioglycolic acid (P-549) (eq. 4). Oxidation yields the corresponding thioindigo dye.



m.p. 200° (4)

(b) **1*H*-Thianaphtheno[3,2-*c*]pyrazole**

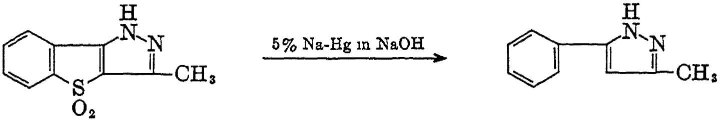
Only substituted derivatives of this series are known. The general method of preparation consists of intramolecular dehydration of a 2-ketophenylhydrazone derivative of thianaphthene (33,190,362) (eq. 5). The



(I) (5)

variations of R and R′ as well as the melting points of this series of compounds are listed in Table VIII-1. It was noted by some of these investigators (362) that sulfur in the thianaphthene ring inhibits the ring-closure step, since similar compounds in the benzenoid series are cyclized without treatment with acid. It was stated that this may be due to the extreme rigidity which the sulfur bridge confers on the molecule, or to the chemical character of the sulfur atom or to a combination of both.

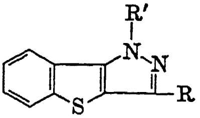
The 4-dioxides (sulfones) of this series are prepared by condensation of the 2-acyl-3-hydroxythianaphthene 1-dioxides with hydrazines (114) or by oxidation of the parent compounds with hydrogen peroxide (33,190,362). The melting points of these compounds are listed in Table VIII-1. Reduction of the 4-dioxide of I ($R = CH_3$, $R' = H$) with sodium amalgam cleaves the thiophene ring to form 3-methyl-5-phenylpyrazole (33) (eq. 6).



(6)

Reduction of the 4-dioxide of I ($R = CH_3$, $R' = C_6H_5$) gives 1,5-diphenyl-3-methylpyrazole and a small amount of 1,5-diphenyl-3-methylpyrazoline.

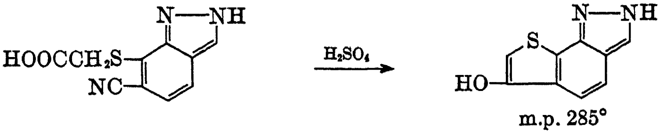
TABLE VIII-1. Melting Points of 1*H*-Thianaphtheno[3,2-*c*]pyrazoles



Substituents	M.p., °C.	M.p., °C., of 1,1-dioxides
$R = CH_3$, $R' = H$	185	244–246
$R = CH_3$, $R' = C_6H_5$	120	180
$R = CH_3$, $R' = 2\text{-}NO_2C_6H_4$	225	242
$R = CH_3$, $R' = 3\text{-}NO_2C_6H_4$	175	185
$R = CH_3$, $R' = 4\text{-}NO_2C_6H_4$	256–258	243
$R = CH_3$, $R' = 2,4\text{-}(NO_2)_2C_6H_3$	279	255
$R = CH_3$, $R' = 2\text{-}CH_3OC_6H_4$	177	202
$R = CH_3$, $R' = 4\text{-}BrC_6H_4$	161	207
$R = C_6H_5$, $R' = C_6H_5$	171	225
$R = CH_3$, $R' = 3\text{-}NO_2\text{-}4\text{-}CH_3C_6H_3$	126	—
$R = CH_3$, $R' = C_6H_5,6\text{-}Cl$	135	265

(c) 2*H*-Thieno[3,2-*g*]indazole

The 6-hydroxy derivative of this system is formed in the usual manner from 6-cyanoindazole-7-thioglycolic acid (P-549,P-196) (eq.7). This



(7)

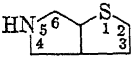
compound is reported to undergo oxidation to the corresponding thioindigo dye.

2-Methyl-6-hydroxy-2*H*-thieno[3,2-*g*]indazole (m.p. 200°) was also prepared by the same method. The thioindigo dye derived from this compound dyes cotton in olive shades.

C. Pyrrole Ring Systems

The majority of the ring systems in this section are indole and carbazole derivatives that have been prepared by the Fischer indole synthesis, which involves the interaction of the keto form of 3-hydroxythiophenes, 3-hydroxythianaphthenes, etc. with arylhydrazones. Since this is a well-known synthesis practiced in the benzenoid series, no discussion of the mechanism is included. A recent reference (619) summarizes the literature on this mechanism and presents kinetic data to substantiate the postulations.

1. *C_4N-C_4S Systems*

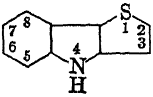


(*Ring Index* No. 643)
5*H*-Thieno[2,3-*c*]pyrrole

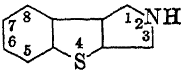
This system is known only as the imide of 2,3-thiophenedicarboxylic acid (353), m.p. 204°, which has been prepared by the action of ammonia on 2,3-thiophenedicarbonyl chloride.

5*H*-Thieno[2,3-*c*]pyrrole is an integral part of the thienoporphyrin system (353) listed below (see section V.b).

2. *C_4N-C_4S-C_6 Systems*



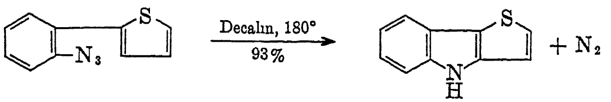
(*Ring Index* No. 1414)
4*H*-Thieno[3,2-*b*]indole



(*Ring Index* No. 1415)
2*H*-Thianaphtheno[2,3-*c*]pyrrole

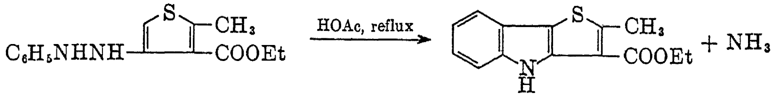
(a) **4*H*-Thieno[3,2-*b*]indole**

A recent synthesis has yielded the parent compound of this system. 2-(2′-Azidophenyl)thiophene when heated eliminates nitrogen and couples at the 3-position of the thiophene nucleus (609) (eq. 8). This colorless carbazole isolog readily forms a brilliant purple picrate.



(8)

3-Carbethoxy-2-methyl-4*H*-thieno[3,2-*b*]indole is formed from 3-carbethoxy-2-methyl-4-phenylhydrazothiophene (I) through a modification of the Fischer indole synthesis (41) (eq. 9). This light yellow solid gives



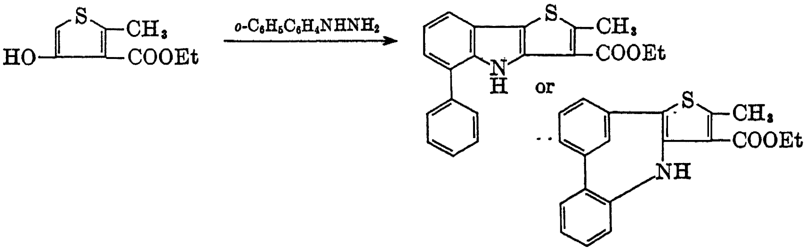
(9)

(I) (II)

a blue-green color with ferric chloride and exhibits chromotropism (red shades) in concentrated H_2SO_4. The free acid is decarboxylated by dry distillation with lime to yield 2-methyl-4*H*-thieno[3,2-*b*]indole (III). 2-Methyl-5,6,7 or 8-substituted derivatives of II and III are prepared by the same condensation employing the properly substituted phenyl group in compound I (84). Table VIII-2 lists the melting points of the compounds prepared in this series.

4-Alkyl derivatives of II are prepared by treating the parent compounds with alkylmagnesium halides or by methyl or ethyl sulfate (84). Compound III yields a 4-nitroso derivative when reacted with nitrous acid.

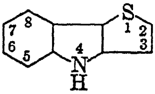
The investigators pointed out that while they believed that the product obtained from *o*-xenylhydrazine was the 5-phenyl derivative of II, an intermolecular dehydrogenation involving both phenyl nuclei might have taken place to give an eight-membered ring system (eq. 10).



(10)

Compound II when brominated with the calculated amount of bromine is said to yield a 7-bromo derivative identical to the product obtained from *p*-bromophenylhydrazine and I.

TABLE VIII-2. Derivatives of 4-Thieno[3,2-*b*]indole

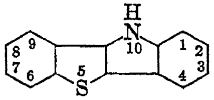


Substituent	M.p., °C.	Ref.
None	175	609
—, picrate	174–175	
2-CH$_3$	154–155	41
2-CH$_3$-4-NO	84–85	41
2-CH$_3$-3-COOH	275–276 (dec.)	41
2-CH$_3$-3-COOC$_2$H$_5$	171–172	41
2,5-(CH$_3$)$_2$	110	84
—, picrate	152	
2,5-(CH$_3$)$_2$-3-COOH	262 (dec.)	84
2,5-(CH$_3$)$_2$-3-COOC$_2$H$_5$	136	84
2,4,5-(CH$_3$)$_3$	B.p. 235–240 (12 mm.)	84
2,5-(CH$_3$)$_2$-4-C$_2$H$_5$	B.p. 235–245 (12 mm.)	84
2,6-(CH$_3$)$_2$	188	84
—, picrate	173	
2,6-(CH$_3$)$_2$-3-COOH	285 (dec.)	84
2,6-(CH$_3$)$_2$-3-COOC$_2$H$_5$	134	84
2,7-(CH$_3$)$_2$	156	84
—, picrate	180	
2,7-(CH$_3$)$_2$-3-COOH	302 (dec.)	84
2,7-(CH$_3$)$_2$-3-COOC$_2$H$_5$	170	84
2,5,6-(CH$_3$)$_3$	165	84
—, picrate	145	
2,5,6-(CH$_3$)$_3$-3-COOH	250	84
2,5,6-(CH$_3$)$_3$-3-COOC$_2$H$_5$	142	84
2-CH$_3$-5-C$_6$H$_5$	156	84
2-CH$_3$-3-COOH-5-C$_6$H$_5$	310 (dec.)	84
2-CH$_3$-3-COOC$_2$H$_5$-5-C$_6$H$_5$	124	84
2-CH$_3$-7-C$_6$H$_5$	160	84
2-CH$_3$-3-COOH-7-C$_6$H$_5$	266	84
2-CH$_3$-3-COOC$_2$H$_5$-7-C$_6$H$_5$	172	84
2-CH$_3$-7-Cl	162	84
—, picrate	152	
2-CH$_3$-3-COOH-7-Cl	325 (dec.)	84
2-CH$_3$-3-COOC$_2$H$_5$-7-Cl	208	84
2-CH$_3$-3-COOC$_2$H$_5$-7-Br	215	84

(b) 2*H*-Thianaphtheno[2,3-c]pyrrole

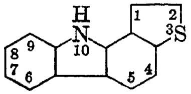
This system is known only as the imide of 2,3-thianaphthenedicarboxylic acid (522,353). This compound's preparation and physical properties are listed in Chapter II (section X.B).

3. *C_4N-C_4S-C_6-C_6 Systems*

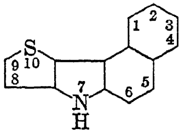


(*Ring Index* No. 2290)

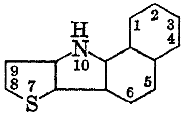
10*H*-Thianaphtheno[3,2-*b*]indole



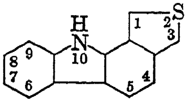
10*H*-Thieno[3,2-*a*]carbazole



7*H*-Benzo[*e*]thieno[3,2-*b*]indole



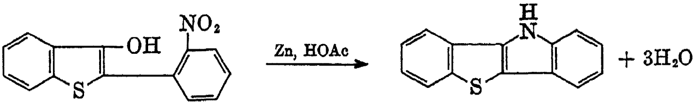
10*H*-Benzo[*g*]thieno[3,2-*b*]indole



10*H*-Thieno[3,4-*a*]carbazole

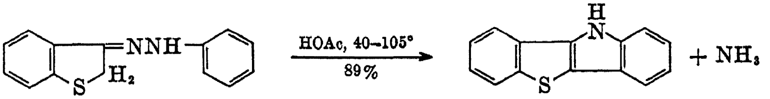
(a) 10*H*-Thianaphtheno[3,2-*b*]indole

The parent compound of this system can be synthesized by two methods. The first method involves reduction of 3-hydroxy-2-(2′-nitrophenyl)-thianaphthene (358) (eq. 11). The second method involves the Fischer indole synthesis with the phenylhydrazone of 3-hydroxythianaphthene (141,358,149,35) (eq. 12). The second method is more widely applied.



(I)

(11)

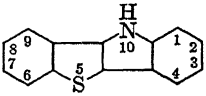


(I)

(12)

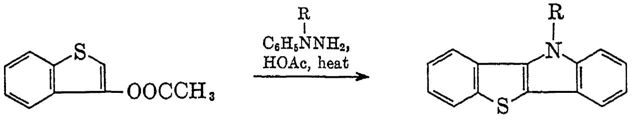
Substitution in the phenyl rings yields the corresponding substituted derivatives (190,360,141). Cohen and Smiles (114) obtained the 5-dioxide of I by the first method. It was later reported that this compound cannot be obtained by the second method (360,190). Dagleish and Mann (141) have noted that the second method *fails* to yield indoles when the thianaphthene ring is substituted in the 4-position. 3-Hydroxythianaphthene does not form an indole with 2,4-dinitrophenylhydrazine and *o*-tolylhydrazine. The investigators could not adduce any steric or electronic reason for the peculiar characteristics of these compounds.

TABLE VIII-3. Melting Points of Derivatives of 10*H*-Thianaphtheno [3,2-*b*]indole



Substituent	M.p., °C.	Ref.
None	252–253	358
—, picrate	171	141
—, styphnate	175–176 (dec.)	141
—, picrolonate	188 (dec.)	141
2- (or 4-) CH_3	256	141
—, picrate	185 (dec.)	141
3-CH_3	257–258	360
6-CH_3	202	141
—, picrate	186–188	141
8-CH_3	211	360
10-CH_3	172–174	360
3,8-$(CH_3)_2$	304	141
6-Cl	223	141
—, picrate	178 (dec.)	141
8-Cl	222	190
3,6-$(CH_3)_2$-8-Cl	241	141
—, picrate	201 (dec.)	141
3,6-$(CH_3)_2$-8-Cl-10-C_2H_5	165	141
—, picrate	129	141
3-Br	262–264	360
10-NO	151–153 (dec.)	141
3-NO_2	350–352 (dec.)	141
7-C_2H_5O	243	141
10-CHO	145	141
—, picrate	148–150 (dec.)	141
10-CH_3CO	160–161	141
10-CH_2CH_2CN	167	141
10-$CH_2CH_2COOC_2H_5$	168	141
5-Dioxide	220	114

The 10-alkyl derivatives of I are obtained by a modification of the second method (360,141) (eq. 13). The 3-hydroxy derivatives or their esters may be used in this reaction.



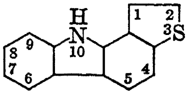
(13)

The melting points of the derivatives of this system are listed in Table VIII-3.

(b) 10*H*-Thieno[3,2-*a*]carbazole

Reaction of phenylhydrazine with 4-oxo-4,5,6,7-tetrahydrothianaphthene or its 2-substituted homologs yields 4,5-dihydro-10*H*-thieno[3,2-*a*]-

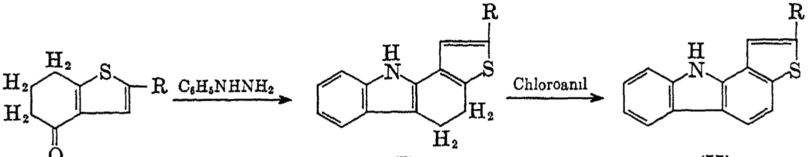
TABLE VIII-4. Derivatives of 10*H*-Thieno[3,2-*a*]carbazole



Substituent	M.p., °C.	4,5-Dihydro deriv., m.p., °C.
None	237	183
2-CH_3	249	178
7-CH_3	264	205
8-CH_3	255	159
—, tetrachlorophthalic anhydride complex	226 (dec.)	
9-CH_3	190	163
—, picrate	208	
10-CH_3	193	
2-C_2H_5	187	
—, tetrachlorophthalic anhydride complex	223	
2,6-$(CH_3)_2$	193	165
2,7-$(CH_3)_2$	Above 300	256
2,8-$(CH_3)_2$	276	208
6,9-$(CH_3)_2$	170	[a]
7,10-$(CH_3)_2$	173	
8,9-$(CH_3)_2$	206	160
2,6,9-$(CH_3)_3$	230	141
7-C_6H_5	244	166
—, picrate	171	
2-Cl	210	130
—, tetrachlorophthalic anhydride complex	220	

[a] Not listed.

carbazoles (I). Dehydrogenation to 10*H*-thieno[3,2-*a*]carbazoles (II) is accomplished by means of chloranil (84,615,624,669) (eq. 14). Homologs



(I) (II)

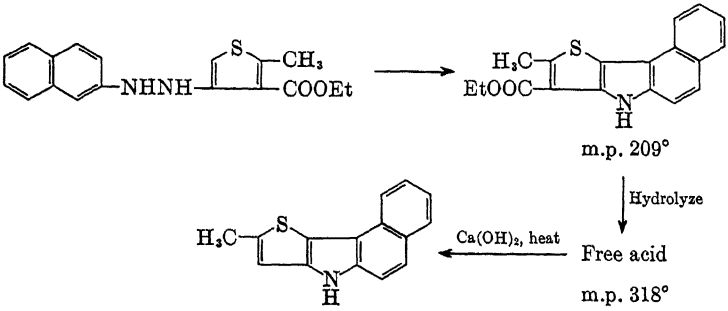
R = H, CH_3, C_2H_5, Cl

(14)

of this system are listed in Table VIII-4 and are obtained by use of substituted phenylhydrazines in eq. 14. Nearly all of the 4,5-dihydro analogs of this series exhibit chromotropism in concentrated sulfuric acid. All form dark violet picrate salts. Orange complexes with tetrachlorophthalic anhydride are described with the 8-methyl, 2-chloro, and 2-ethyl derivatives (750).

(c) 7*H*-Benzo[*e*]thieno[3,2-*b*]indole

This system is formed from the reaction of 2-naphthylhydrazine with 3-carbethoxy-4-hydroxy-2-methylthiophene (84) (eq. 15). Compound I forms a picrate, m.p. 175°.



(I)
m.p. 152°

(15)

(d) 10*H*-Benzo[*g*]thieno[3,2-*b*]indole

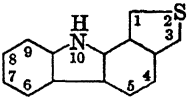
As in the isomeric system directly above, this system can be prepared by reacting 3-carbethoxy-4-hydroxy-2-methyl-thiophene with 1-naphthylhydrazine (84). The original compound, 9-carbethoxy-8-methyl-10*H*-benzo[*g*]thieno[3,2-*b*]indole, melts at 142°; the free acid melts at 320°

8-Methyl-10*H*-benzo[*g*]thieno[3,2-*b*]indole melts at 165° and forms a picrate melting at 184°.

(e) 10*H*-Thieno[3,4-*a*]carbazole

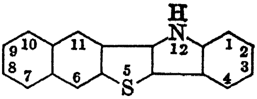
This system arises by the indolization of 1,3-dimethyl-4,5,6,7-tetrahydroisothianaphthene-4-one by the method demonstrated in eq. 14 (624). The derivatives are listed in Table VIII-5.

TABLE VIII-5. Derivatives of 10*H*-Thieno[3,4-*a*]carbazole (624)

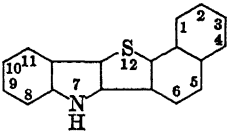


Substituents	M.p., °C.	4,5-Dihydro deriv., m.p., °C
1,3-$(CH_3)_2$	175	—
1,3,6-$(CH_3)_3$	148	—
1,3,7-$(CH_3)_3$	199	187
1,3,8-$(CH_3)_3$	154	132
1,3,6,7-$(CH_3)_4$	194	—
1,3,6,9-$(CH_3)_4$	175	—

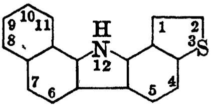
4. *C_4N-C_4S-C_6-C_6-C_6 Systems*



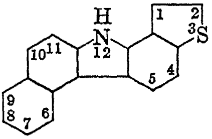
12*H*-Benzo[5,6]thianaphtheno[3,2-*b*]indole



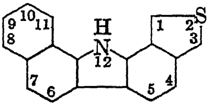
7*H*-Benzo[6,7]thianaphtheno[3,2-*b*]indole



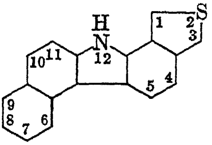
12*H*-Benzo[*i*]thieno[3,2-*a*]carbazole



12*H*-Benzo[*g*]thieno[3,2-*a*]carbazole



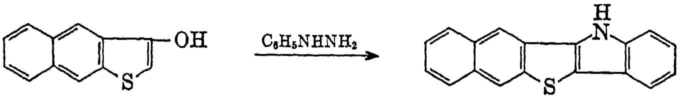
12*H*-Benzo[*i*]thieno[3,4-*a*]carbazole



12*H*-Benzo[*g*]thieno[3,4-*a*]carbazole

(a) 12*H*-Benzo[5,6]thianaphtheno[3,2-*b*]indole

Condensation of 3-hydroxythiophanthrene (3-hydroxynaphtho[2,3-*b*]-thiophene) with phenylhydrazine yields the parent compound of this ring system (141) (eq. 16).

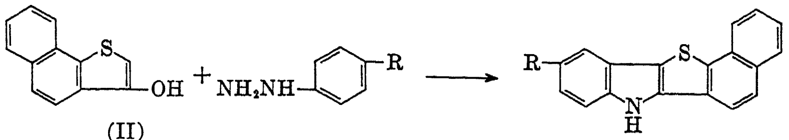


Pale green, m.p. 358°

(16)

(b) 7*H*-Benzo[6,7]thianaphtheno[3,2-*b*]indole

The basic ring system of this series results from the condensation of 3-hydroxynaphtho[1,2-*b*]thiophene (II) with phenylhydrazine (141). When *p*-substituted phenylhydrazines are employed, 10-substituted derivatives result (eq. 17). Both compounds III and V are reported to form dipicrates (m.p. 178–180° (dec.) and 186–187° (dec.), respectively). The 7-methyl derivative of III, m.p. 226°, results when phenylmethylhydrazine is employed in the ring-closure step. It also forms a dipicrate, m.p. 165°. An attempted synthesis of the 8-methyl derivative with *p*-tolylhydrazine and II failed.



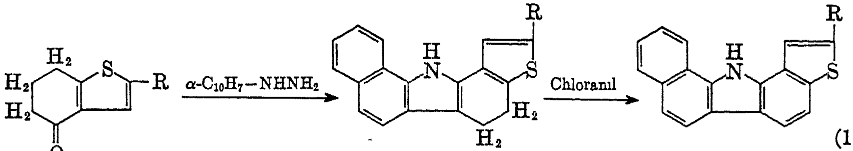
(II)

(17)

(III), R = H, m.p. 325–326°
(IV), R = CH_3, m.p. 318°
(V), R = CH_3, m.p 380–382°

(c) 12*H*-Benzo[*i*]thieno[*3*,2-*a*]carbazole

Buu-Hoï and coworkers (84,615,624,669) have prepared this basic ring system and some of its homologs by condensing 4-oxo-4,5,6,7-tetrahydrothianaphthene and its 2-substituted homologs with 1-naphthylhydrazine (eq. 18).



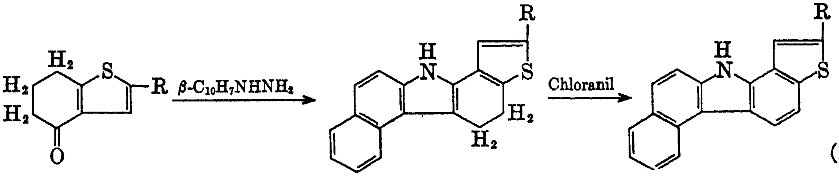
(18)

R = H, m.p. 225°
R = CH_3, m.p. 215°
R = C_2H_5, m.p. 140°
R = Cl, m.p. 106°

R = H, m.p. 232°
R = CH_3, m.p. 234°
R = C_2H_5, m.p. 170°
R = Cl, m.p. 206°

(d) 12*H*-Benzo[*g*]thieno[3,2-*a*]carbazole

The reaction of 4-oxo-4,5,6,7-tetrahydrothianaphthene and its 2-substituted homologs with 2-naphthylhydrazine yields the 4,5-dihydrobenzo[*g*]thieno[3,2-*a*]carbazole, which is subsequently dehydrogenated to the completely aromatic system (84,615,624,669) (eq. 19).



(19)

R = H, m.p. 213–214°
R = CH_3, m.p. ——
R = C_2H_5, m.p. 175°
R = Cl, m.p. 180°

R = H, m.p. 223°
R = CH_3, m.p. 233°
R = C_2H_5, m.p. 209°
R = Cl, m.p. 227°

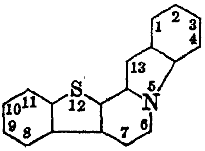
(e) **12*H*-Benzo[*i*]thieno[3,4-*a*]carbazole**

The 1,3-dimethyl derivative of this system (m.p. 234°) was obtained from treating the corresponding 4,5-dihydro derivative (m.p. 215°) with chloranil by the method demonstrated in eq. 18. The starting ketone was 4-oxo-1,3-dimethyl-4,5,6,7-tetrahydroisothianaphthene (624).

(f) **12*H*-Benzo[*g*]thieno[3,4-*a*]carbazole**

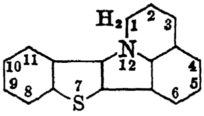
The 1,3-dimethyl derivative of this system (m.p. 233°) was obtained from treating the 4,5-dihydro derivative with chloranil by the method demonstrated in eq. 19. The starting ketone was 4-oxo-1,3-dimethyl-4,5,6,7-tetrahydroisothianaphthene (624).

5. C_4N-C_4S-C_5N-C_6-C_6 Systems



(*Ring Index* No. 2971)

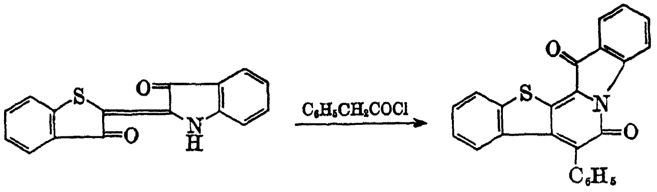
Benzo[*b*]thianaphtheno[3,2-*g*]pyrrocoline



1*H*-Thianaphtheno[2,3-*d*]quino[1,8-*ab*]pyrrole

(a) **Benzo[*b*]thianaphtheno[3,2-*g*]pyrrocoline**

The German patent literature (P-379) describes the condensation of phenylacetyl chloride with 2-thianaphthene-2′-indole indigo. The resultant compound is said to have the structure of 6,13-dioxo-7-phenylbenzo[*b*]thianaphtheno[3,2-*g*]pyrrocoline (eq. 20). According to the claims of this



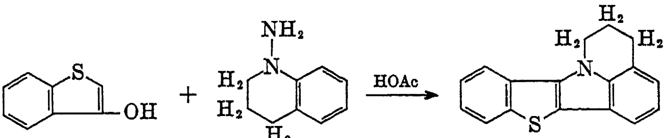
(20)

(I) (II)

patent this reaction can be carried out with derivatives of I and arylated fatty acid halides.

(b) **1*H*-Thianaphtheno[2,3-*d*]quino[1,8-*ab*]pyrrole**

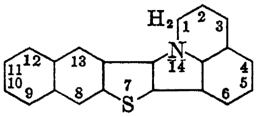
The only example of this series is the 1*H*-2,3-dihydrothianaphtheno[2,3-*d*]quino[1,8-*ab*]pyrrole which results from the Fischer indole synthesis when 3-hydroxythianaphthene is condensed with 1-amino-1,2,3,4-tetrahydroquinoline (141) (eq. 21).



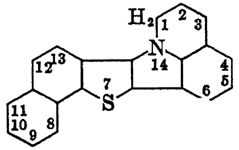
(21)

(III)
m.p. 139°
Picrate, m.p. 149°

6. C_4N-C_4S-C_5N-C_6-C_6-C_6 Systems



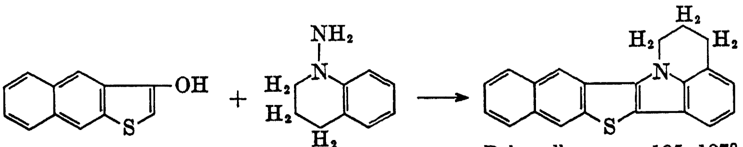
1*H*-Benzo[5,6]thianaphtheno[3,2-*b*]pyrid[3,2,1-*hi*]indole



1*H*-Benzo[6,7]thianaphtheno[3,2-*b*]pyrid[3,2,1-*hi*]indole

(a) **1*H*-Benzo[5,6]thianaphtheno[3,2-*b*]pyrid[3,2,1-*hi*]indole**

Condensation of 3-hydroxythiophanthrene and 1-amino-1,2,3,4-tetrahydroquinoline yields the 1,2,3-trihydro derivative of this system (141) (eq. 22).

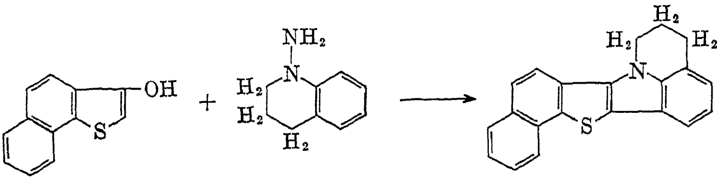


(22)

Pale yellow, m.p. 195–197°

(b) 1*H*-Benzo[6,7]thianaphtheno[3,2-*b*]pyrid[3,2,1-*hi*]indole

Condensation of 3-hydroxynaphtho[1,2-*b*]thiophene and 1-amino-1,2,3,4-tetrahydroquinoline yields the 1,2,3-trihydro derivative of this system (141) (eq. 23).



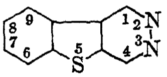
(23)

m.p. 237°
Dipicrate, m.p. 184°

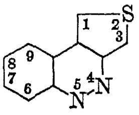
II. Diazine Ring Systems

A. Pyridazine Ring Systems (1,2-Diazines)

1. C_4S-C_4N_2-C_6 Systems



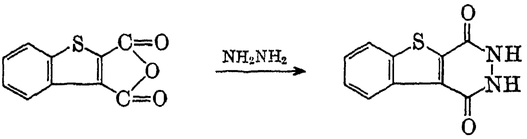
Thianaphtheno[2,3-*d*]pyridazine



(*Ring Index* No. 1732)
Thieno[3,4-c]cinnoline

(a) Thianaphtheno[2,3-*d*]pyridazine

1,4-Dioxo-1,2,3,4-tetrahydrothianaphtheno[2,3-*d*]pyridazine is the only example of this series. It is prepared by reacting hydrazine with 2,3-thianaphthenedicarboxylic anhydride (301) (eq. 24). This material gives an orange color with ferric chloride. It also forms an acetyl derivative, m.p. 195–196°.

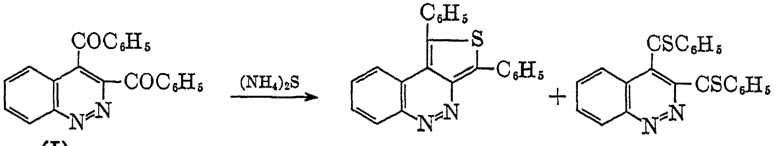


(24)

m.p. 360–361°

(b) Thieno[3,4-c]cinnoline

1,3-Diphenylthieno[3,4-*c*]cinnoline is said to form in low yield during the formation of the dithioketone of 3,4-dibenzoylcinnoline I (7) (eq. 25).

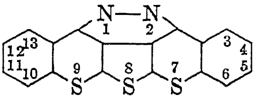


(I)

(25)

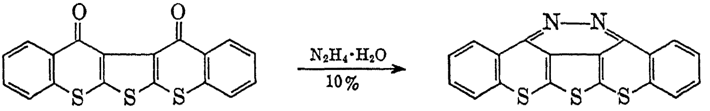
The cedar-yellow crystalline compound, m.p. 151°, is reconverted to compound I by the action of nitric acid.

2. C_4S-C_4N_2-C_5S-C_5S-C_6-C_6 Systems



(*Ring Index* No. 3534)

No systematic name has been assigned to the ring system that results from the condensation of hydrazine hydrate with 12,13(2*H*)-thieno[2,3-*b*,5,4-*b*′]bis[1]benzothiapyran-12,13-dione (478) (eq. 26). The original investigators referred to this compound as $\alpha,\beta,\alpha',\beta'$-thiophenobis(thiochromone)azine.

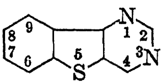


Blue-violet, m.p. 298–299°

(26)

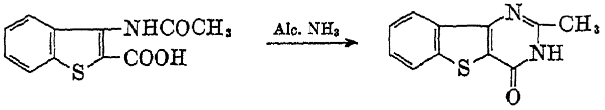
B. Pyrimidines (1,3-Diazines)

1. C_4S-C_4N_2-C_6 Systems



Thianaphtheno[3,2-*d*]pyrimidine

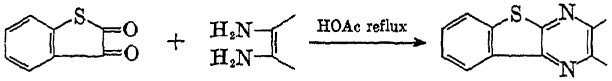
2-Methyl-4-oxo-3,4-dihydrothianaphtheno[3,2-*d*]pyrimidine is the only example of the pyrimidine ring system. It has been prepared from the reaction of 3-acetamido-2-thianaphthenecarboxylic acid and alcoholic ammonia (363) (eq. 27).



(27)

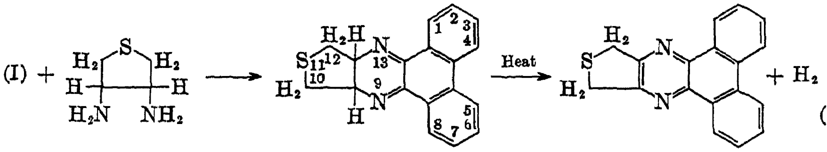
C. Pyrazines (1,4-Diazines)

Members of this series of compounds are all formed by a common method *i.e.*, the condensation of thianaphthenequinones with an orthodiamine (eq. 28). The ring systems which have been prepared and the physical properties of the individual compounds are listed in Table VIII-6. With a few exceptions, these compounds can be considered as quinoxaline derivatives containing a thiophene ring system.



(28)

In one isolated case, phenanthroquinone (I) and 3,4-diaminothiacyclopentane (II) are said to react to form hydrogenated products of this ring system (616) (eq. 29). A corresponding 10-valeric acid derivative of IV (m.p. 202–204°) was obtained from the diamino acid from biotin (3,4-diaminotetrahydrothiophene-2-valeric acid). This reaction was instrumental in assigning the 2-position to the —$(CH_2)_4COOH$ group of biotin.

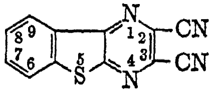
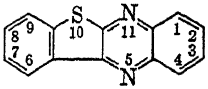
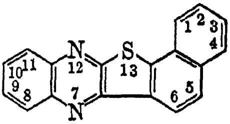
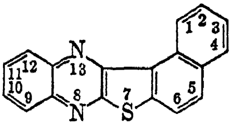
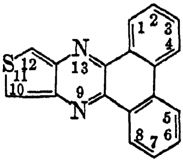


(29)

(II) (III) (IV)

9a,10,12,12a-Tetrahydro-
dibenzo[*f*,*h*]thieno[3,4-*b*]-
quinoxaline · red, m.p. 183–185°

TABLE VIII-6. Condensed Thiophene Compounds Containing Pyrazine Rings

Compound and name	Ref.	M.p., °C.	Comments[a]
$C_4S—C_4N_2—C_6$  2,3-Dicyanothianaphtheno[3,2-*b*]pyrazine	P-149	211–212	When heated with CuBr in C_5H_5N gives a golden-green complex
$C_4S—C_4N_2—C_6—C_6$  Thianaphtheno[2,3-*b*]quinoxaline	46	166–167	Colorless crystals
$C_4S—C_4N_2—C_6—C_6—C_6$  *Ring Index* No. 3122 Naph[2′,1′,4,5]thieno[2,3-*b*]quinoxaline	155	277	Concd. H_2SO_4, brown
9-(or 10-) chloro-10-(or 9-) methyl derivative	155	266	Concd. H_2SO_4, brownish-red Wool dyed greenish yellow
 *Ring Index* No. 3132 Naph[1′,2′,4,5]thieno[2,3-*b*]quinoxaline	155	205	Concd. H_2SO_4, blue
10-(or 11-) chloro-11-(or 10-) methyl derivative	155	271	Concd. H_2SO_4, blue Wool dyed greenish yellow
 Dibenzo[*fh*]thieno[3,4-*b*]quinoxaline	616	—	See discussion in text

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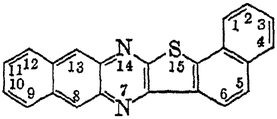
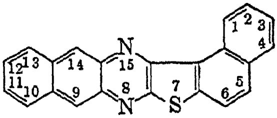
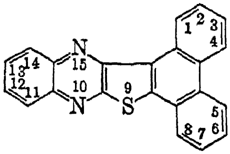
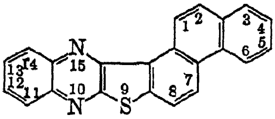
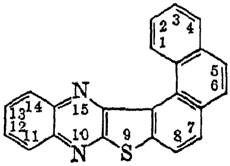
[a] Colors on wool are produced from the acid bath.

Table continued

TABLE VIII-6 (*continued*)

Compound and name	Ref.	M.p., °C.	Comments[a]
$C_4S-C_4N_2-C_6-C_6-C_6-C_6$			
 *Ring Index* No. 3535 Benzo[*g*]naph[2′,1′,4,5]thieno-[2,3-*b*]quinoxaline	155	246	Concd. H_2SO_4, blue Wool dyed bright yellow
 *Ring Index* No. 3536 Benzo[*g*]naph[1′,2′,4,5]thieno-[2,3-*b*]quinoxaline	155	237	Concd. H_2SO_4, violet Wool dyed bright brown
 Phenanthro[9′,10′,4,5]thieno-[2,3-*b*]quinoxaline	165	255	Yellow crystals Concd. H_2SO_4, green
12-(or 13-) chloro-13-(or 12-) methyl derivative	165	271	Concd. H_2SO_4, blue
 Phenanthro[2′,1′,4,5]thieno-[2,3-*b*]quinoxaline	703	274	Golden yellow Concd. H_2SO_4, green Wool, light yellow
 Phenanthro[3′,4′,4,5]thieno-[2,3-*b*]quinoxaline	703	287	Yellow Concd. H_2SO_4, violet Wool, pale yellow

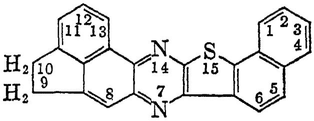
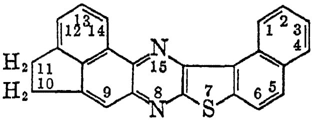
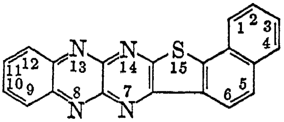
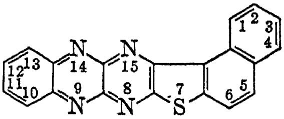
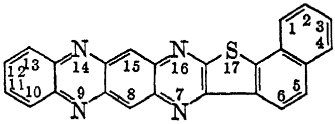
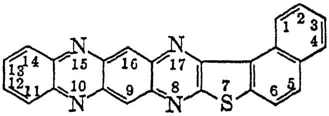
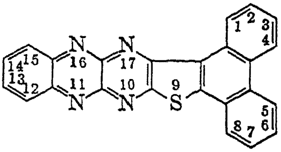
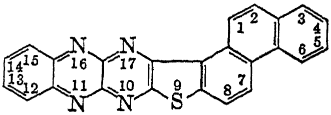
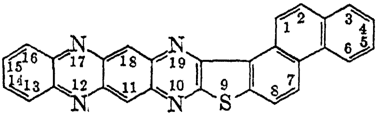
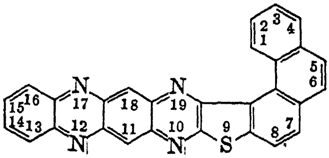
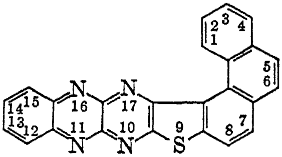
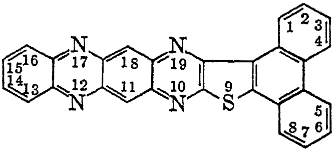
Compound and name	Ref.	M.p., °C.	Comments[a]
$C_4S—C_5—C_4N_2—C_6—C_6—C_6—C_6$			
 *Ring Index* No. 3703 Acenaphtho[4,5-*b*]naph[2′,1′,4,5]thieno-[2,3-*e*]pyrazine	155	272	Concd. H_2SO_4, blue Wool dyed bright brown
 *Ring Index* No. 3704 Acenaphtho[4,5-*b*]naph[1′,2′,4,5]thieno-[2,3-*e*]pyrazine	155	248	Concd. H_2SO_4, greenish blue Wool dyed tan
$C_4S—C_4N_2—C_4N_2—C_6—C_6—C_6$			
 *Ring Index* No. 3532 Naph[2′,1′,4,5]thieno[2,3-*b*]quinoxalo-[2,3-*e*]pyrazine	155	Above 295	Concd. H_2SO_4, rose Wool dyed brown
 *Ring Index* No. 3533 Naph[1′,2′,4,5]thieno[2,3-*b*]quinoxalo-[2,3-*e*]pyrazine	155	Above 295	Concd. H_2SO_4, bluish-black Wool dyed orange-red
$C_4S—C_4N_2—C_4N_2—C_6—C_6—C_6—C_6$			
 *Ring Index* No. 3738 Naph[1′,2′,4,5]thieno[2,3-*b*]quinoxalo-[2,3-*g*]quinoxaline	155	Above 295	Concd. H_2SO_4, bluish black Wool dyed chocolate brown

Table continued

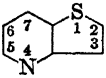
TABLE VIII-6 (*continued*)

Compound and name	Ref.	M.p., °C.	Comments[a]
 *Ring Index* No. 3739 Naph[2′,1′,4,5]thieno[2,3-*b*]quinoxalo-[2,3-*g*]quinoxaline	155	Above 295	Concd. H_2SO_4, brownish-violet Wool dyed brownish-violet
 Phenanthro[9′,10′,4,5]thieno-[2,3-*b*]quinoxalo[2,3-*e*]pyrazine	165	233–234	Red crystals Concd. H_2SO_4, violet
 Phenanthro[2′,1′,4,5]thieno-[2,3-*b*]quinoxalo[2,3-*e*]pyrazine	703	230	Red Concd. H_2SO_4, violet Wool, orange-yellow
$C_4S—C_4N_2—C_4N_2—C_6—C_6—C_6—C_6—C_6$			
 Phenanthro[2′,1′,4,5]thieno-[2,3-*b*]quinoxalo[2,3-*g*]quinoxaline	703	Above 290	Red Concd. H_2SO_4, greenish blue Wool, orange-yellow
 Phenanthro[3′,4′,4,5]thieno-[2,3-*b*]quinoxalo[2,3-*g*]quinoxaline	165	Above 290	Chocolate brown crystals Concd. H_2SO_4, bluish-black

Compound and name	Ref.	M.p., °C.	Comments[a]
 Phenanthro[3′,4′,4,5]thieno-[2,3-*b*]quinoxalo[2,3-*e*]pyrazine	703	Above 290	Chocolate Concd. H_2SO_4, blackish-violet Wool, chocolate
$C_4S—C_4N_2—C_4N_2—C_6—C_6—C_6—C_6—C_6$			
 Phenanthro[9′,10′,4,5]thieno-[2,3-*b*]quinoxalo[2′,3-*g*]quinoxaline	703	Above 290	Chocolate Concd. H_2SO_4, green Wool, chocolate

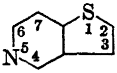
III. Pyridine Ring Systems

A. C_4S-C_5N Systems



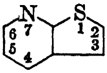
(*Ring Index* No. 848)

Thieno[3,2-*b*]pyridine



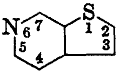
(*Ring Index* No. 849)

Thieno[3,2-*c*]pyridine

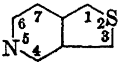


(*Ring Index* No. 850)

Thieno[2,3-*b*]pyridine



Thieno[2,3-*c*]pyridine



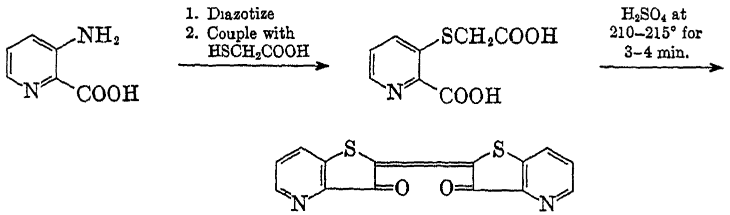
(*Ring Index* No. 851)

Thieno[3,4-*c*]pyridine

Of the above five systems of this series, the only parent compound known is thieno[2,3-*b*]pyridine. The other isomers are known only as their derivatives. The chemistry of this series of compounds has not been studied, and for this reason a particularly promising field of research is still open to investigators. It would be of particular interest to compare the reactivity of the thiophene ring of thianaphthene to these systems to ascertain the influence of a nitrogen atom on the resonance of the condensed thiophene ring. In reverse order, it would be of interest to determine the influence of the sulfur atom on the reactions of quinoline; *e.g.*, would the action of phenyl lithium yield a lithium derivative or would it add at the nitrogen atom as in the quinoline series?

1. *Thieno[3,2-b]pyridine*

A thioindigo type dye has been synthesized that contains this basic ring system. The final compound apparently is formed from an unstable intermediate 3-hydroxythieno[3,2-*b*]pyridine which can be synthesized by the usual thioglycolic acid ring closure (408,407) (eq. 30). This indigoid dye is dark violet and decomposes at 300–330° without melting. In sulfuric acid, it is dark blue. Tin and acid reduce it to a leuco compound which tints wool in rose shades from an acid bath. The dye is decolorized with hot 20% hydrochloric acid and hydrogen sulfide is evolved. Reduction in the hydrosulfite vat destroys the color with evolution of hydrogen sulfide. This indicates exceptional instability of the thiophene ring caused by the presence of the nitrogen atom in the adjacent ring, since compounds of the thianaphthene series are stable to such treatment.



"δ-Thiopyrindigo"

(30)

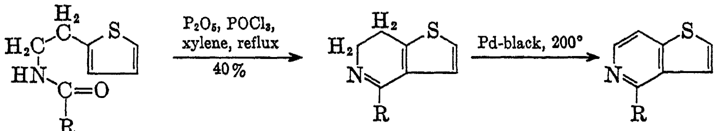
Note added in proof: Two recent publications (771,772) describe the preparation of the 3-hydroxy derivative and its conversion into several derivatives isosteric to 8-hydroxy and 8-aminoquinoline. These derivatives are tabulated in Table VIII-7. The original article (772) should be consulted for antimalarial activity.

TABLE VIII-7. Derivatives of Thieno [3,2-*b*]pyridine

Derivative	B.p., °C. (mm.)	M.p., °C.
3-Cl		99
3-NH_2		92
sec-3,3′-NH		188–190
3-$NHCH_2CH_2NEt_2$	166–169 (1 8)	
—, citrate salt		153 (dec.)
3-$NHCH_2CH_2CH_2NEt_2$	171–174 (2)	
—, citrate salt		110 (dec.)
3-$NHCH(CH_3)CH_2CH_2CH_2NEt_2$	176–180 (1)	
—, citrate salt		82 (dec.)
3-OH		146–148
—, HCl salt		168–170
—, methiodide salt		190 (dec.)
3,3′-oxide		221–222
—, HCl salt		295–298
3-$OOCCH_3$	143–145 (2.0–2.5) n_D^{20} 1 6104 n_D^{26} 1 6072 d^{25} 1.325	
3-$OOCC_6H_5$		96
3-OH-2(?)-I		138–139

2. Thieno[3,2-c]pyridine

The Bischler-Napieralski synthesis of isoquinoline has been applied to this thiophene system. The 4-substituted isoquinoline isosteres result in fair yields by this method (612) (eq. 31).



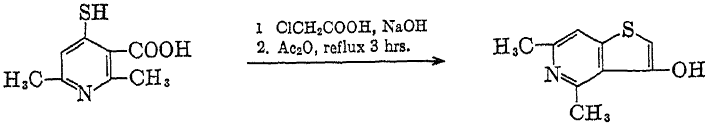
(I) (II)

(31)

I: R = CH_3, b.p. below 140° at 0.5 mm.; picrate, m.p. 204° (dec.).
R = C_6H_5, b.p. 149–152° at 0.5 mm.; picrate, m.p. 165° (dec.)
II: R = CH_3, b.p. 86° at 1 mm.; picrate, m.p. 245.5–246° (dec.).
R = C_6H_5, b.p. 140–160° at 0.5 mm.; picrate, m.p. 175° (dec.).

Compounds of type II are reported to have typical quinoline odors.

Members of this class of compounds have also been prepared through a ring-closure synthesis involving the thioglycolic acid derivative of a pyridine (323) (eq. 32). This compound forms a crystalline hydrochloride, m.p.



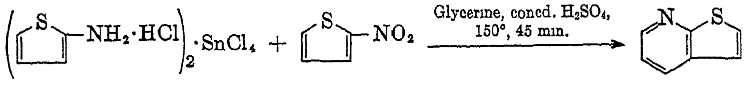
(32)

Orange, m.p. 49°

94°. It reacts with semicarbazide to form a rose-red semicarbazone that decomposes at about 300°. It couples with *p*-toluenediazonium chloride to give a 2(?)-substituted dark-brown azo dye, m.p. 98°. When dissolved in alkali solution, the compound is oxidized by air at 75° to the corresponding thioindigo dye. This dye is an orange-colored solid subliming at 360° at 15 mm. pressure. The thioindigo dye is reduced to a pale yellow-colored leuco base in the hydrosulfite bath or with tin and hydrochloric acid. Apparently the thiophene ring system of this series is more stable than that of the prior series where ring rupture occurred in these processes.

3. Thieno[2,3-b]pyridine

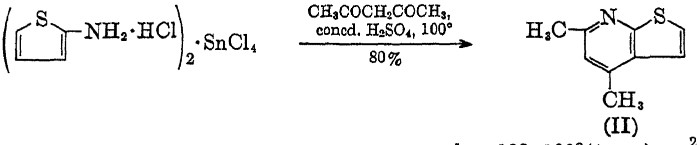
This compound has been prepared from 2-aminothiophene and 2-nitrothiophene in very low yield by means of the Skraup synthesis (465,466) (eq. 33). Compound I is reported to have an odor like quinoline. It



(33)

(I)

forms a greenish-yellow picrate, m.p. 185°; a yellow methiodide derivative, m.p. 198.5°; and a tan complex with chromic acid containing two moles of I to one of acid. A cornflower-blue complex of similar constitution is obtained with cobalt chloride.

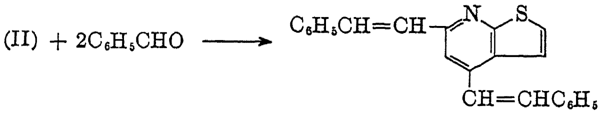


(34)

(II)

b.p. 103–108° (4mm.); n_D^{20} 1.6320; d_{20}^{20} 1.152

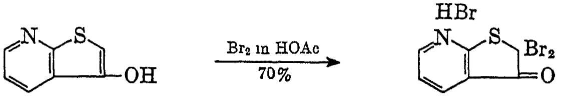
4,6-Dimethylthieno[2,3-*b*]pyridine is prepared in good yield by the condensation of acetylacetone with 2-aminothiophene (177) (eq. 34). Zinc chloride or phosphorus pentoxide can also be employed as condensation catalysts. Compound II yields a hydrochloride salt (m.p. 241–242° (dec.)), a methiodide (m.p. 228–229° (dec.)), and a picrate (m.p. 190–191°). When reacted with benzaldehyde, a 4,6-dibenzylidene derivative is formed (eq. 35).



(35)

(III)
m.p. 238°
HCl, m.p. 268°

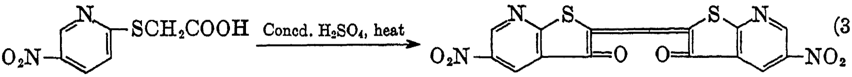
3-Hydroxythieno[2,3-*b*]pyridine, from 2-pyridylthioglycolic acid and boiling acetic anhydride, is a yellow solid, m.p. 182° (322). (*Note:* Recent investigators (716) have questioned the authenticity of this structure.) It can be oxidized by air in sodium hydroxide solution or by potassium ferricyanide to a red-brown thioindigo derivative. When treated with bromine, a yellow hydrobromide salt of 2,2-dibromo-3-oxo-2,3-dihydrothieno-[2,3-*b*]pyridine is formed (eq. 36). The free base is a dark-yellow oil which forms a chloroplatinate derivative, m.p. 171°.



(36)

m.p. 185°

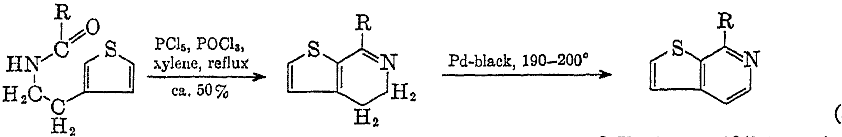
The 5-nitro derivative of 2-pyridylthioglycolic acid is converted by means of concentrated sulfuric acid to an unstable violet thioindigoid dye (115) (eq. 37).



(37)

4. *Thieno[2,3-c]pyridine*

Herz (608) has successfully applied the Bischler-Napieralski synthesis of isoquinolines to this thiophene system. 7-Substituted derivatives are obtained by the following series of reactions (eq. 38). The compounds are reported to have typical quinoline odors.



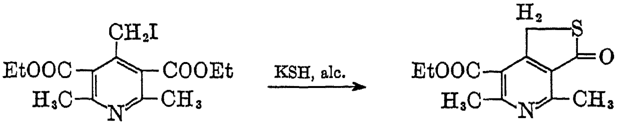
(38)

R = CH_3, b p. 75° (1–2 mm.) picrate, m.p. 191° (dec.)
R = C_6H_5, oil picrate, m p. 165° (dec.)

R = C_6H_5, b.p. 150° (0.5 mm.) picrate, m.p. 156° (dec.)

5. Thieno[3,4-c]pyridine

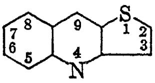
3-Oxo-4,6-dimethyl-7-carbethoxythieno[3,4-*c*]pyridine and the 7-carboxy derivative are the only compounds known in this series. The former is synthesized by reaction 39 (42). The pale brown free acid, obtained by saponification, melts at 272° (dec.).



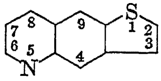
(39)

Pale red, m.p. 115–116°

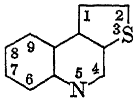
B. C_4S-C_5N-C_6 Systems



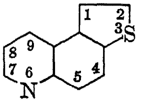
(*Ring Index* No. 1733)
Thieno[3,2-*b*]quinoline



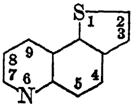
(*Ring Index* No. 1734)
Thieno[2,3-*g*]quinoline



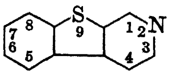
(*Ring Index* No. 1735)
Thieno[2,3-*c*]quinoline



(*Ring Index* No. 1736)
Thieno[3,2-*f*]quinoline



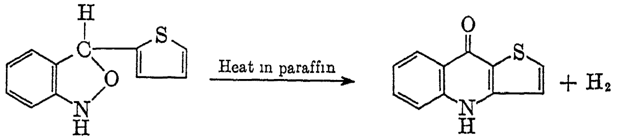
Thieno[2,3-*f*]quinoline



Thianaphtheno[2,3-*c*]pyridine

1. *Thieno[3,2-b]quinoline*

The 9-oxo derivative of this heterocycle is obtained from heating 2-thienylanthranil in paraffin (476). The yield is said to be very low (eq. 40).

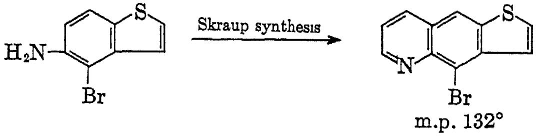


(40)

The orange-colored product melts at about 320° and shows considerable bluish-black fluorescence in concentrated solutions of acids and in alcoholic potassium hydroxide.

2. *Thieno[2,3-g]quinoline*

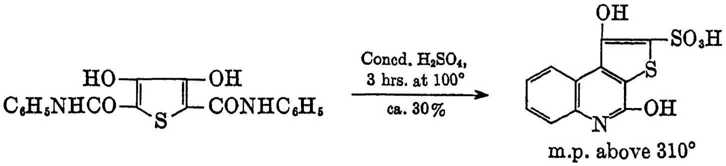
This ring system results from the application of the Skraup synthesis to 5-amino-4-bromothianaphthene (222). The resultant compound is 4-bromothieno[2,3-*g*]quinoline (eq. 41). Note that in the Skraup synthesis with 5-aminothianaphthene (eq. 43), the ring closure takes place at the 4-position rather than at the 6-position.



(41)

3. *Thieno[2,3-c]quinoline*

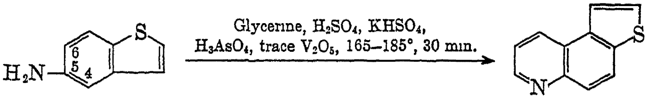
The action of concentrated sulfuric acid on 2,5-bis(carboxanilido)-3,4-dihydroxythiophene yields a compound, thought by the investigator (230) to be a sulfonic acid derivative of 2,4-dihydroxythieno[2,3-*c*]quinoline. The known replacement of carbonyl radicals at the 2-position on the thiophene nucleus by the —SO_3H radical (see *Thiophene and Its Derivatives*, p. 421) leads the present authors to assign the 2-position to the sulfonic acid group (eq. 42). This compound forms hydrochloride and hydrobromide salts which melt above 300°.



(42)

4. Thieno[3,2-f]quinoline

When 5-aminothianaphthene is subjected to the Skraup synthesis, fusion takes place at the 4,5-position and the resultant ring system is thieno[3,2-*f*]quinoline (222) (eq. 43). Apparently the yield was fairly good,


H$_2$N
S
6
5
4
Glycerine, H$_2$SO$_4$, KHSO$_4$,
H$_3$AsO$_4$, trace V$_2$O$_5$, 165–185°, 30 min.
S
N

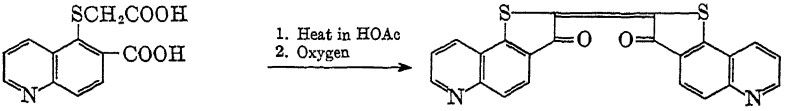
m.p. 88°

(43)

since the reaction was carried out on only 0.7 g. of starting material and several tests were made with the resultant product. When the 4-position is blocked (see eq. 41), ring closure occurs at the 6-position, yielding the isomeric ring system, thieno[2,3-*g*]quinoline.

5. Thieno[2,3-f]quinoline

This ring system occurs only in a thioindigo type dye which was formed by the usual thioindoxyl type synthesis, involving the corresponding *o*-carboxyquinolylthioglycolic acid (375) (eq. 44).

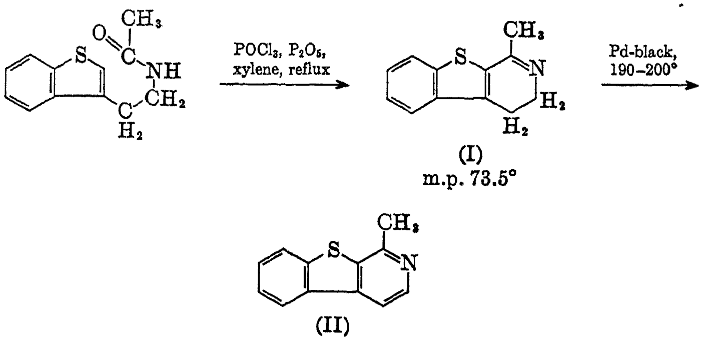


m.p. 400–410°

(44)

6. Thianaphtheno[2,3-c]pyridine

The most recent addition to the C$_4$S-C$_5$N-C$_6$ systems is the isoquinoline synthesis carried out on 3-(2-acetamidoethyl)thianaphthene by Herz



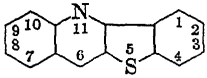
(I)
m.p. 73.5°

(45)

(II)
m.p. 110°

(608). The intermediate, 1-methyl-3,4-dihydrothianaphtheno[2,3-*c*]pyridine, was dehydrogenated to the fully aromatic ring system with palladium black (eq. 45). Both compounds I and II form picrates which melt with decomposition at 227–228° and 262°, respectively. The 1-phenyl derivative of I is formed when 3-(2-benzamidoethyl)thianaphthene is employed in the original reaction. This compound melts at 64° and gives a picrate, m.p. 196–198° (dec.). The dehydrogenation to the 1-phenyl derivative of II was not reported.

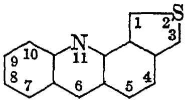
C. C_4S-C_5N-C_6-C_6 Systems



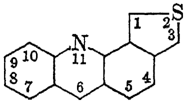
(*Ring Index* No. 2501)

Thianaphtheno[3,2-*b*]quinoline

Thiaquindoline



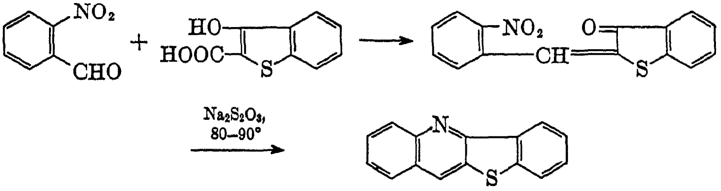
Thieno[2,3-*c*]acridine



Thieno[3,4-*c*]acridine

1. *Thianaphtheno[3,2-b]quinoline (Thiaquindoline)*

This heterocycle is obtained by an interesting sequence of reactions which further demonstrate the ease of replacement of groups in the 2-position of thianaphthene. Thus, when 3-hydroxythianaphthene-2-carboxylic acid is warmed with *o*-nitrobenzaldehyde, the respective 2-benzylidine derivative (a thioindogenide) is obtained (398). Reduction of this compound with sodium hyposulfite yields the cyclized product (I) (eq. 46).

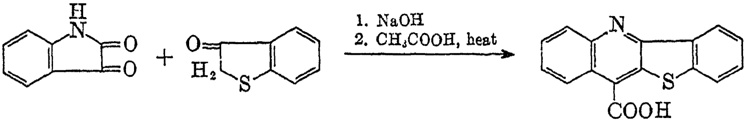


(46)

(I)
Colorless, m.p. 169°

Compound I is reported to be a somewhat weaker base than quindoline, its pyridine isostere. However, it is reported to form hydrochloride and picrate salts which decompose upon contact with water. Compound I dyes wool, silk, and tannin-mordanted cotton fabrics yellow from an acid bath. The shades are somewhat feebler than those imparted by quindoline. The original literature should be consulted for description of colors produced by these two compounds with dimethyl sulfate.

The 6-carboxy derivative of this system is produced by the standard Pfitzinger reaction with isatin (399) (eq. 47). Compound II is a yellow



(II)

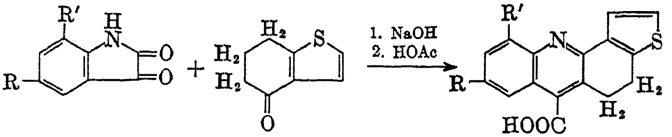
(47)

product melting at about 335°. This compound dyes wool, silk, and mordanted cotton yellow from an acid bath. The original literature should be consulted for the variety of shades produced by the metallic salts of **II** and a comparison of the colors produced by the isosteres where the S atom is replaced by CO, CH_2, and NH.

2. Thieno[2,3-c]acridine

Through an unfortunate set of circumstances this system appears in the original literature and subsequent abstracts as the thieno[3,2-*c*]acridine system (79). This error arose from assigning the wrong structure to the starting compound, 4-oxo-4,5,6,7-tetrahydrothianaphthene. Thus, the original investigators (79) assigned the structure 7-oxo-4,5,6,7-tetrahydrothianaphthene to the product prepared by cyclizing 4-(2-thienyl)butyric acid by the method of Fieser and Kennelly (184) (see Chapter II, section III.C for details of this preparation).

4-Oxo-4,5,6,7-tetrahydrothianaphthene reacts with isatin and benzenoid-substituted isatins to yield the respective 4,5-dihydro-6-carboxy



(III)

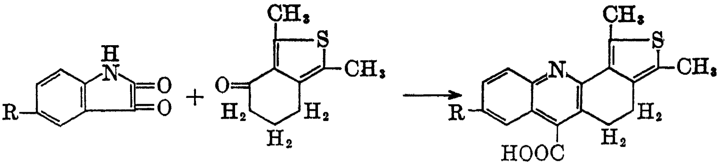
(48)

(IIIa); R = R′ = H; m.p. 321–322° (dec.)
(IIIb); R = CH_3; R′ = H; m.p. 310° (dec.)
(IIIc); R = R′ = CH_3; m.p. 247° (dec.)
(IIId); R = Br; R′ = H; m.p. 270° (dec.)

derivatives of thieno[2,3-*c*]acridine (79) (eq. 48). Compounds IIIa–c were decarboxylated to yield the respective 4,5-dihydrothieno[2,3-*c*]-acridines, (IV); IVa, m.p. 141–142°, picrate, m.p. 221–222° (dec.); IVb, m.p. 171°, picrate, m.p. 180–181°. Compound IVb when heated with lead dioxide at 310° yields the fully aromatic compound, 8-methylthieno[2,3-*c*]-acridine, m.p. 179–180°. The picrate of this material decomposes above 250°. The 2-chloro derivative of IIIa (m.p. 262–263° dec.) is formed by the condensation of isatin with 2-chloro-4-oxo-4,5,6,7-tetrahydrothianaphthene (625). The 2-methyl derivatives of IIIa (m.p. 325° dec.) and IIId (m.p. 325–326°) have been prepared from 2-methyl-4-oxo-4,5,6,7-tetrahydrothianaphthene (624).

3. Thieno[3,4-c]acridine

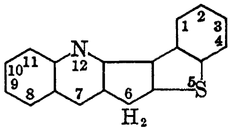
Derivatives of this system arise by the condensation of isatin with 1,3-dimethyl-4-oxo-4,5,6,7-tetrahydroisothianaphthene (624) (eq. 49). When



(49)

R is H the resultant compound sublimes at 257–259°; where R is Br the melting point is above 330°. The latter compound is decarboxylated at 330°.

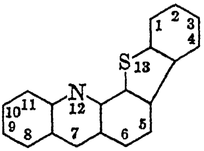
D. C_4S-C_5-C_5N-C_6-C_6 Systems



6*H*-Quinolino[3,2-*b*]thianaphtheno[3,2-*d*]cyclopentadiene

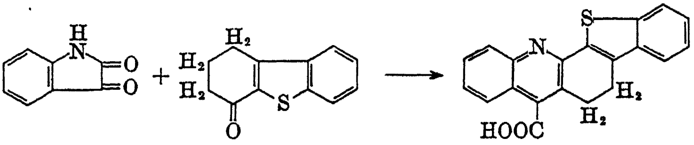
The Pfitzinger reaction, when carried out with 3-oxo-1,2,3-trihydrocyclopenta[3,2-*b*]thianaphthene and isatin, yields the 7-carboxy derivative of this heterocycle (90). This compound is decarboxylated at its melting point (300°) and yields the basic ring system 6*H*-quinolino[3,2-*b*]thianaphtheno[3,2-*d*]cyclopentadiene, m.p. 225.5°; picrate, m.p. 250° (dec.).

E. C_4S-C_5N-C_6-C_6-C_6 Systems



Thianaphtheno[3,2-*c*]acridine

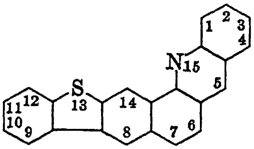
The 7-carboxy-5,6-dihydro derivative of this system arises from the Pfitzinger reaction between 4-oxo-1,2,3,4-tetrahydrodibenzothiophene and isatin (77) (eq. 50). Heating of I *in vacuo* yields the decarboxylated derivative, 5,6-dihydrothianaphtheno[3,2-*c*]acridine (II), b.p. 250° (1 mm.), m.p. 202–203°. Compound II forms a picrate, m.p. 205°. Heating of II with lead dioxide at 320° yields the fully aromatic system, m.p. 172°; picrate, m.p. 213–215° (dec.).



(50)

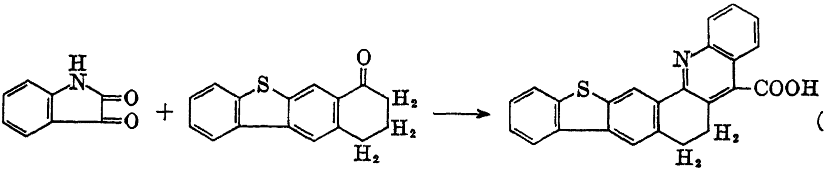
(I)
m.p. above 320°

F. C_4S-C_5N-C_6-C_6-C_6-C_6 Systems



Thianaphtheno[2′,3′,4,5]benz[1,2-*c*]acridine

Derivatives of this system arise in a manner similar to that shown directly above for thianaphtheno[2,3-*c*]acridine by condensation of isatin with

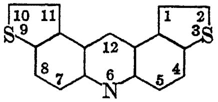


(51)

m.p. above 325°

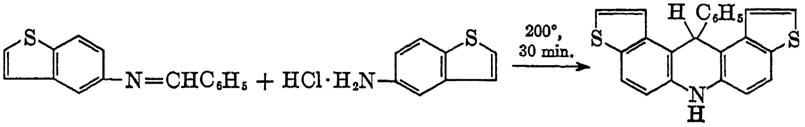
the appropriate ketone system (77) (eq. 51). Decarboxylation and subsequent dehydrogenation to the basic ring system were not reported.

G. C_4S-C_4S-C_5N-C_6-C_6 Systems



(*Ring Index* No. 2988)
Dithieno[3,2-*a*,2′,3′-*j*]acridine

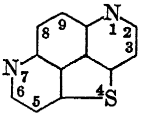
The 6,12-dihydro-12-phenyl derivative of this heterocycle is prepared by an interesting condensation between 5-aminothianaphthene hydrochloride and the benzylidene derivative of 5-aminothianaphthene (222) (eq. 52). This synthesis is somewhat similar to the benzoflavine and Brilliant Acridine Orange syntheses which involve benzaldehyde and activated aniline systems.



(52)

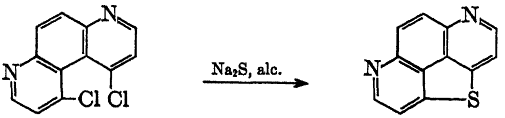
(I) bronze, m.p. 269°

H. C_4S-C_5N-C_5N-C_6 Systems



(*Ring Index* No. 2500)
Thieno[*lmn*][4,7]phenanthroline

The parent compound of this system results when 4,5-dichloro-1,8-phenanthroline (I) is reacted with sodium sulfide (P-580, P-251) (eq. 53).



(53)

(I)

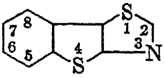
(II)
m.p. 186–187°

The 2,6-dimethyl derivative of II, m.p. 229–231°, was also prepared by this method from the 2,7-dimethyl derivative of I.

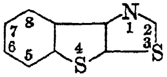
Thiourea when condensed with I evolves hydrogen chloride and compound II results from the intermediate thiouronium salt.

IV. N,S and N,O Ring Systems

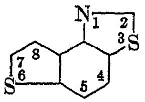
A. Thiazoles Containing C_4S-C_3NS-C_6 Systems



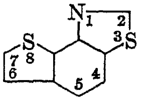
Thianaphtheno[2,3-*d*]thiazole



Thianaphtheno[3,2-*d*]thiazole



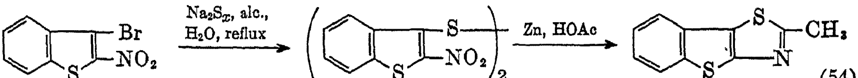
Thianaphtheno[4,5-*d*]thiazole



Thianaphtheno[7,6-*d*]thiazole

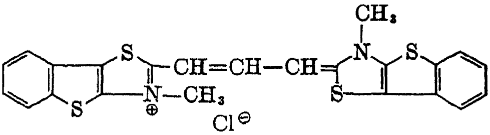
1. *Thianaphtheno[2,3-d]thiazole*

The 2-methyl derivative of this system was prepared from 3-bromothianaphthene (P-598,P-600) (eq. 54). Compound I is converted to a blue dye composition by means of dimethyl sulfate and ethyl chloroformate in the presence of pyridine. Its structure is said to be represented by the following formula:



(I) Crystalline, no m.p. given

(54)

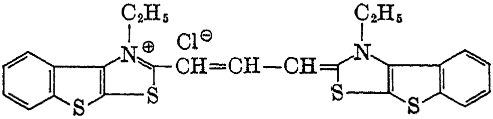


(II)

Compound II, as well as its isomer below, is reported to be useful as a photographic sensitizer (P-600).

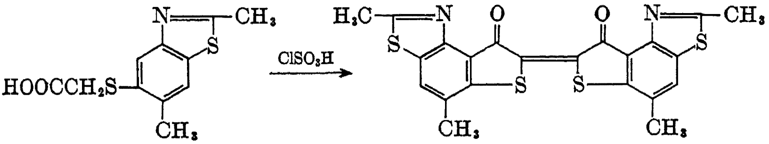
2. *Thianaphtheno[3,2-d]thiazole*

The 2-methyl derivative of this system (III) is prepared by almost exactly the same procedure as I (see eq. 54) with the exception that the starting material is 3-nitrothianaphthene which is brominated to produce the isomeric intermediate, 2-bromo-3-nitrothianaphthene (P-598,P-600). Compound III is an oil and can be converted to the *N*-ethyl homolog of the isomer of II by heating with diethyl sulfate and ethyl chloroformate in pyridine and then finally treating with ammonium chloride. The structure of this black amorphous powder was represented by the following formula (IV).


(IV)

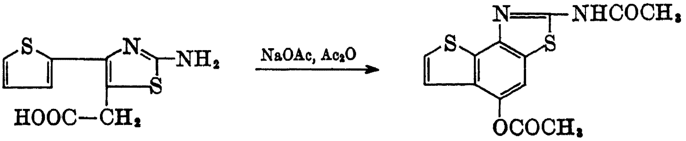
3. *Thianaphtheno[4,5-d]thiazole*

This system is known only as the corresponding thiazolethioindigo dye. It is formed when 2,6-dimethylbenzothiazole-5-thioglycolic acid is treated with chlorosulfonic acid (424). Undoubtedly the 8-hydroxy derivative is formed as an intermediate in this reaction (eq. 55). This dye colors fibers in bluish-green shades.


(55)

4. *Thianaphtheno[7,6-d]thiazole*

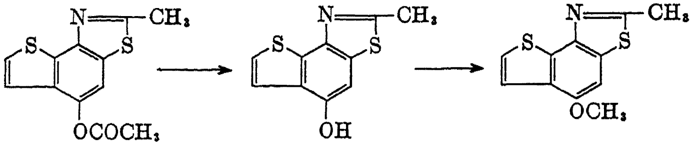
This heterocycle is known only in the form of derivatives. The system is formed by heating 2-amino-4-(2′-thienyl)-5-thiazoleacetic acid in the presence of acetic anhydride and sodium acetate (321) (eq. 56). The 2-


(56)

(I)

(II) Cream colored, m.p. 285–289°

methyl-5-acetoxy derivative of this system (III) results from the same type of ring closure with 2-methyl-4-(2′-thienyl)-5-thiazoleacetic acid. Compound III can be converted to the 5-hydroxy derivative (IV), which in turn can be methylated to give the 5-methoxy derivative (V) (eq. 57).



(III) m.p. 130–130.5°

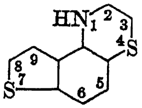
(IV) m.p. 268° (subl.)

(V) m.p. 127.5–128°

(57)

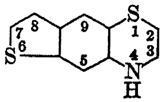
Complex derivatives of this system are patented as improvers in photographic emulsions and in the manufacture of photosensitive dyes (P-677).

B. *p*-Thiazines Containing C_4S-C_4NS-C_6 Systems



(*Ring Index* No. 1731)

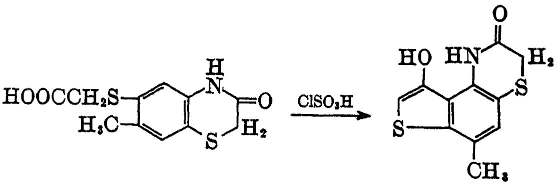
1*H*-Thianaphtheno[5,4-*b*]-*p*-thiazine



4*H*-Thianaphtheno[5,6-*b*]-*p*-thiazine

1. *1H-Thianaphtheno[5,4-b]-p-thiazine*

Derivatives of this heterocyclic system result when 4*H*-3-oxo-7-methylbenzo-*p*-thiazine-6-thioglycolic acid is condensed in the usual manner (424) (eq. 58). This greenish-blue material can be converted to the cor-



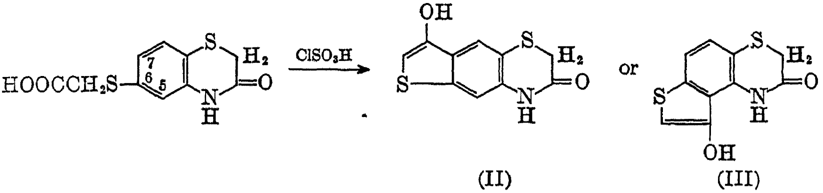
(I)

(58)

responding thioindigo dye which gives bluish-green colors when applied to fibers.

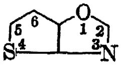
2. 4H-Thianaphtheno[5,6-b]-p-thiazine

This system arises in much the same manner as compound I above from 4*H*-3-oxobenzo-*p*-thiazine-6-thioglycolic acid (40). The original investigator indicated that ring closure occurred at carbon 7 to form compound II. However, it is difficult to see why cyclization could not occur equally well at carbon 5 to form III (eq. 59). Compound II is rust-red in color, has no reported melting point, and is converted to an intense violet thioindigo derivative.



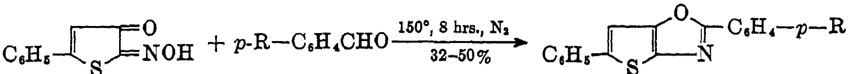
(II) (III) (59)

C. Thieno[2,3-*d*]oxazole



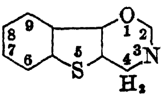
Thieno[2,3-*d*]oxazole

Derivatives of this system arise from condensation of aromatic aldehydes with 2-oximino-3-oxo-5-phenylthiophene (758) (eq. 59a).

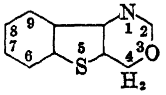


R = H, m.p. 176.2–176.8° (59a)
R = CH_3O, m.p. 166.6–166.9°
R = $(CH_3)_2CH$, m.p. 131.8–132.6°

D. *m*-Oxazines Containing C_4S-C_4NO-C_6 Systems



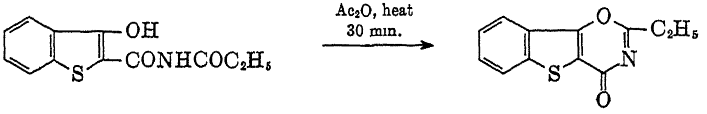
4*H*-Thianaphtheno[2,3-*e*]-*m*-oxazine



4*H*-Thianaphtheno[3,2-*d*]-*m*-oxazine

1. *4H-Thianaphtheno[2,3-e]-m-oxazine*

The only reported compound of this system is 2-ethyl-4*H*-thianaphthen[2,3-*e*]-*m*-oxazine-4-one which is prepared by the following reaction (363) (eq. 60).

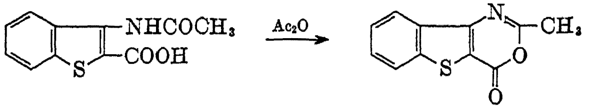


m.p. 209°

(60)

2. *4H-Thianaphtheno[3,2-d]-m-oxazine*

The simplest derivatives of this system are prepared by heating 3-acetamido-2-thianaphthenecarboxylic acid with acetic anhydride (363) (eq. 61).

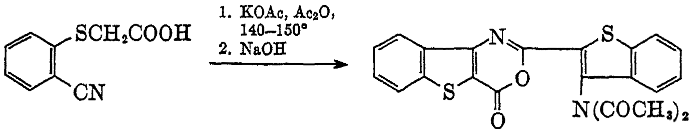


(II)

(61)

Compound II, 2-methyl-4*H*-thianaphtheno[3,2-*d*]-*m*-oxazin-4-one, melts at 179°. Its 2-ethyl homolog prepared from the 3-propionamido-2-thianaphthenecarboxylic acid melts at 209°.

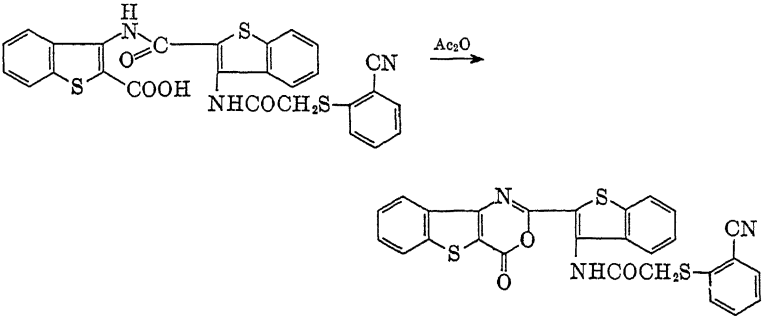
More complex derivatives of this system result from the reaction of *o*-cyanophenylthioglycolic acid with acetic anhydride (eq. 62). The monoacetyl derivative of III, which results from treatment with ammonia, melts at 312°, and when treated with propionic anhydride gives the corresponding *N*-acetyl-*N*-propionyl amide, m.p. 230°. Another complex system also arises from treatment of a thianaphthene derivative with acetic anhydride (eq. 63).



(III)

Yellow, m.p. 259°

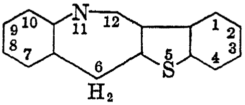
(62)



(63)

V. Macro Nitrogen Ring Systems

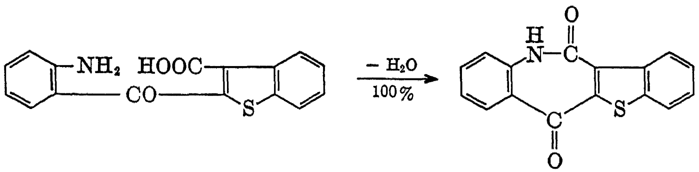
A. C_4S-C_6-C_6-C_6N Systems



(*Ring Index* No. 2577)

6*H*-Benzo[*b*]thianaphtheno[2,3-*e*]azepine

The system is formed as the 6,12-dioxo derivative by warming 2-(2′-aminobenzoyl)-3-thianaphthenecarboxylic acid with acetic anhydride (378) (eq. 64).

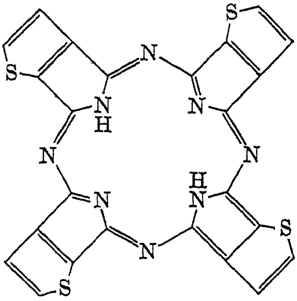


(64)

Yellow, m.p. 312–313°

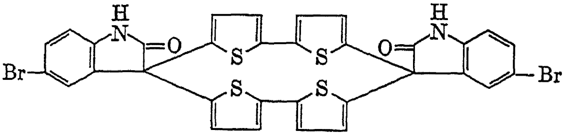
B. C_4S-C_4S-C_4S-C_4S-C_4N-C_4N-C_4N-C_4N-C_8N_8

This heterocyclic porphyrazine results when 2,3-thiophenedicarbonitrile is heated with cuprous chloride (formula shown on page 446). The resultant copper tetra-2,3-thienoporphyrazine is a greenish-blue powder (353). The pigment is said to exhibit a greener shade when thiophene replaces the phenyl group in this series of dyes.



C. C_4S-C_4S-C_4S-C_4S-C_4N-C_4N-C_6-C_6-$C_{10}S_4$

The authenticity of this system is doubtful. It is used by Steinkopf and Roch (599) to represent the compound obtained from bromoisatin and dithienyl in the presence of zinc chloride (see discussion on Indophenine, Chapter III).



(*Ring Index* No. 3904)

Cyclic bis-β-indolidene-bis-α-dithienyl

D. Macro Ring Systems of Doubtful Structure

A number of macro ring systems are reported by Steinkopf, *et al.* (485) to represent the products obtained from dialdehydes of the thiophene series with diamino compounds. It seems more than likely that these materials are linear polymers rather than the cyclic systems suggested by the investigators. All of the compounds are amorphous solids that decompose without melting. The original literature may be consulted for the formulas given.

CHAPTER IX

Condensed Selenophene and Tellurophene Systems

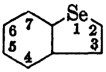
Introduction

This short chapter completes the coverage of selenophene and tellurophene systems begun in *Thiophene and Its Derivatives* (700). Only a minor amount of research has been carried out with these systems. Komppa has studied halogenation, nitration, and acylation reactions of selenonaphthene, but has not established the position of the entering group. Presumably, the 3-position is substituted as in the case of thianaphthene. In support of this postulation, it is pointed out in *Thiophene and Its Derivatives* (p. 479) and in Chapter I of this volume, that heavier atoms of periodic group VIB (Se and Te) have less directing influence on entering substituents than the lower members of the group (O and S). It is recognized that, in electrophilic substitution reactions, 3-substitution of thianaphthene is accompanied by concurrent 2-substitution while benzofuran yields only 2-substitution. It therefore seems reasonable that the amount of 3-substitution of selenonaphthene will be even greater than that which occurs with thianaphthene.

In the case of selenonaphthene, 3-hydroxyselenonaphthene has been prepared by an authentic ring-closure method. Its reactions have been studied in relationship to 3-hydroxythianaphthene and the thioindigo dyes. The selenoindigo dyes are discussed in Chapter III. With the exception of selenonaphthene, the three isomeric selenophthenes (selenophenoselenophenes), dibenzoselenophene, and dibenzotellurophene, the other compounds listed in this chapter are no more than laboratory curiosities, having been prepared only in minute quantities.

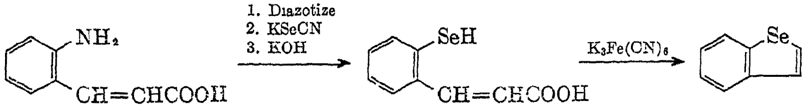
I. Carbocyclic Condensed Selenophene Systems

A. Selenonaphthene



(*Ring Index* No. 855)

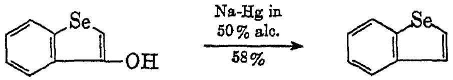
Mazza and Solazza (379) found that selenonaphthene occurred along with selenophene when acetylene was burned in the presence of selenium. Umezawa (511) later noted that this reaction also yielded the selenophthenes (selenophenoselenophenes) which are discussed below. This investigator established the structure of the acetylene-selenium product by an authentic synthesis previously employed for thianaphthene (eq. 1). A



(1)

mixed melting point of this compound and the product obtained from selenium and acetylene showed no depression.

Reduction of 3-hydroxyselenonaphthene with sodium amalgam appears to be the best method of producing selenonaphthene. Komppa and Nyman (330) effected this reaction in 58% yield (eq. 2). These authors

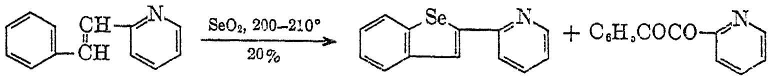


(2)

are the only ones that have investigated the chemical properties. They found that selenonaphthene forms picrate and styphnate complexes by the usual procedures. Bromine water yields a dibromo derivative, while a monobromo derivative was isolated after bromination in chloroform solution. Chlorine in carbon tetrachloride yielded a trichloro derivative. Both the monobromo derivative and the trichloro derivative formed crystalline picrates. The first two positions of substitution are more than likely the 2- and 3-positions. The third position of substitution on the benzenoid portion of the molecule has not been determined in the thianaphthene series, so it cannot be predicted here other than to indicate that the 5-position is the more likely.

Nitration of selenonaphthene with acetyl nitrate yields nitroselenonaphthene. Acylation of selenonaphthene was effected by the usual Friedel-Crafts procedure employing aluminum chloride and acetyl chloride in carbon disulfide solution. The acetyl derivative formed a semicarbazone and could be oxidized to the monocarboxylic acid by means of sodium hypobromite. As in the case of thianaphthene, benzilic acid was condensed with selenonaphthene to form diphenylselenonaphthenyl acetic acid. The physical properties of these compounds are listed in Table IX-1.

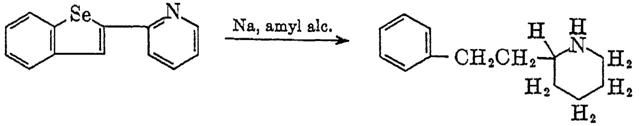
When *sym*-phenyl-2-pyridylethylene (α-stilbazole) is heated with selenium dioxide, 2-(2′-pyridyl)selenonaphthene results (629), and in addition phenyl α-pyridyl diketone is formed (eq. 3). A better yield is obtained



(3)

when *sym*-phenyl-4-pyridylethylene is employed. In this case, no diketone is produced and only the 2-(4′-pyridyl)selenonaphthene results.

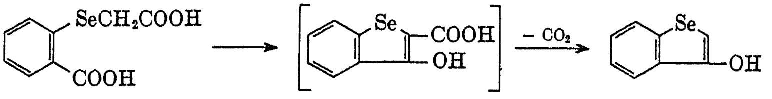
The structures of these materials were established by reductive cleavage of the selenophene ring with sodium in alcohol which resulted in the formation of phenylpiperidylethanes (eq. 4).



(4)

Both 2-(2′-pyridyl)- and 2-(4′-pyridyl)selenonaphthene yield a monobromo derivative when treated with bromine in carbon tetrachloride. Presumably these are the respective 3-bromo derivatives. In each case, an intermediate bromine addition complex was obtained, which when treated with sodium hydroxide, yielded the resultant monobromo derivative. The red 2-pyridyl bromine addition product melted at 185°; the yellow 4-pyridyl product melted at 225°.

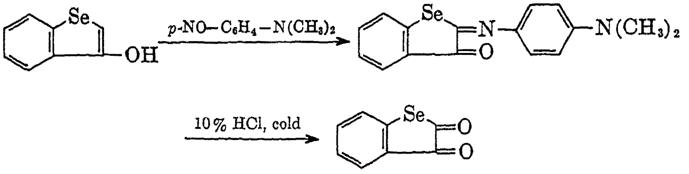
3-Hydroxyselenonaphthene has been prepared by the conventional cyclization methods employed for 3-hydroxythianaphthene. For example, *o*-carboxyphenylselenoacetic acid can be condensed by fusion with caustic at 200° (346) or by refluxing in acetic anhydride (348,441,P-469,P-132,P-702) (eq. 5). The intermediate 2-carboxy-3-hydroxy derivative was too unstable to isolate in the caustic fusion method.



(5)

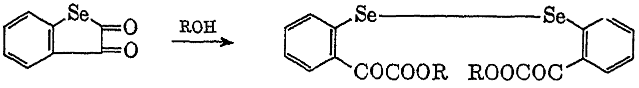
Lesser and coworkers made no effort to establish whether or not this compound exists in the enol or keto form, although they illustrated the compound only in the keto form in their publications. It was noted, however, that in contrast to 3-hydroxythianaphthene, bromination yielded only a 2-monobromo derivative, whereas a 2,2-dibromo derivative of the keto form was expected. In other reactions with aromatic aldehydes (to form benzylidenes), nitrosobenzenes (to form anils), and nitrous acid (to form the 2-oximes) the material appeared to react quite similarly to 3-hydroxythianaphthene (347,348,441). With isatin, acenaphthoquinone, and other dye-forming substances, the resultant selenoindigo dyes formed with an ease equal to the thioindigos. Various modifications of the selenoindigo dyes are discussed in Chapter III. *p*-Nitrophenyldiazonium chloride couples (presumably in the 2-position) with 3-hydroxyselenonaphthene to give an azo dye of red-brown color.

2,3-Selenonaphthenequinone has been prepared from 3-hydroxyselenonaphthene by another standard method employed in the thianaphthene series (eq. 6). In addition to undergoing the usual reactions discussed



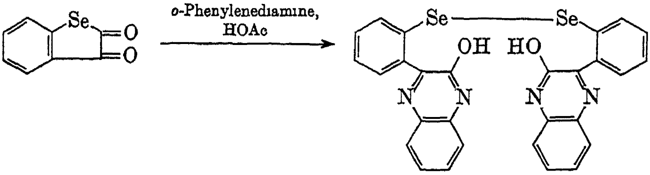
(6)

under 2,3-thianaphthenequinone to form dyestuffs, water or methanol causes ring rupture to form di-*o*-selenophenylglyoxalic acid or its methyl ester (347,441) (eq. 7). The compound does not appear to react as a typical



(7)

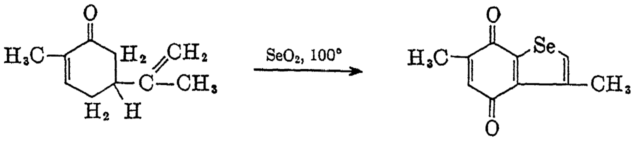
o-quinone, and instead of the expected quinoxaline derivative with *o*-phenylenediamine, an open-chain compound is formed (eq. 8). This hydroxy-



(8)

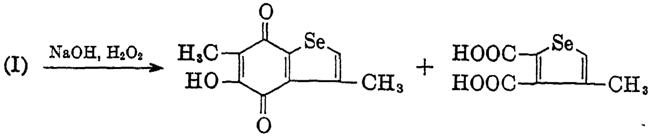
quinoxaline derivative can be methylated with dimethyl sulfate in the usual manner, or it will form esters by reaction with acyl halides. Similar ring ruptures do not appear to occur when the compound is reacted with 3-hydroxythianaphthene or 3-hydroxyselenonaphthene, and the corresponding indigo dyes are obtained.

When carvone is heated on a steam bath with selenium dioxide, 3,6-dimethyl-4,7-selenonaphthenequinone is said to be formed in low yield (614) (eq. 9). Compound I forms a yellow monoxime and a 2,4-dinitrophenylhydrazone. Reduction with hydrogen (palladium on carbon catalyst) yields the 4,7-dihydroxy derivative. When brominated, it is reported to form the 2,5-dibromo derivative. Oxidation with hydrogen peroxide yields the 5-hydroxy derivative as well as 4-methyl-2,3-selenophenedicar-



(I)

(9)



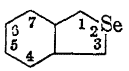
(II)

(10)

boxylic acid (eq. 10). Compound II yields a 5-methoxy derivative when treated with diazomethane and a 5-acetoxy derivative when reacted with acetic anhydride. Reduction with hydrogen (palladium on charcoal catalyst) yields the colorless 3,6-dimethyl-4,5,7-trihydroxyselenonaphthene. Compound II undergoes a rearrangement to the 4,5-quinone when treated with *o*-phenylenediamine, and a quinoxaline derivative fused at the 4,5-positions results (see section II below). The above compounds were discussed in the original literature from the standpoint of possible antivitamin K activity, but no specific test data were recorded.

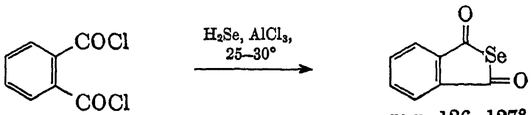
The physical constants of hydroxyselenonaphthenes and selenonaphthenequinones are listed in Table IX-1. A few of the properties of the dyestuffs derived from 3-hydroxyselenonaphthene are listed in Chapter III.

B. Isoselenonaphthene



(*Ring Index* No. 856)

The parent compound, isoselenonaphthene, is not known. The only derivative reported is 1,3-dioxoisoselenonaphthene. This compound is prepared from phthaloyl chloride and hydrogen selenide (501) (eq. 11). It is

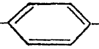
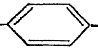
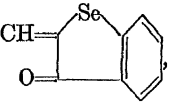


m.p. 126–127°

(11)

reported to decompose in the presence of water, acids, or alkalis with formation of elementary selenium.

TABLE IX-1. Selenonaphthene and Its Derivatives

Substituent	M.p., °C.	Ref.	Deriv.	M.p., °C.	Ref.
None	50–51	330,511	Picrate	156–157	330,379
	53–54	379	Styphnate	146–147	330
Trichloro	B.p. 143 (8 mm.)	330	Picrate	135–136	330
Bromo	B.p. 286–289 (768 mm.)	330	Picrate	128–129	330
Dibromo	129–130	330	—	—	—
Nitro	97	330	—	—	—
Acetyl	91–93	330	Semicarbazone	254–256	330
Carboxylic acid	270–280 (dec.)	330	—	—	—
Diphenylcarboxylic acid	254–255	330	—	—	—
2-(2′-Pyridyl)	142	629	3-Bromo	125	629
2(4′-Pyridyl)	187	629			
3-Hydroxy	76–77	346	2- =NOH, yellow	154–155	348,441
		P-469,P-132	2- $=NOCH_3$, yellow	146–147	348,441
		441	2- $=NOOCCH_3$, yellow	177–178	348,441
			2- $=NOOCC_6H_5$, yellow	184–185	348,441
			2-N=NC_6H_5, orange-red	207–208	348,441
			2- =N—  —$N(CH_3)_2$, green	166–167	348,441
			2-Anil orange form	145–146	348,441
			2-Anil garnet-red form	145–146	348,441
			2-N=N—  —NO_2, red-brown	239–241 (dec.)	347
			2- =CH—CH=  , violet-red	299–300	247

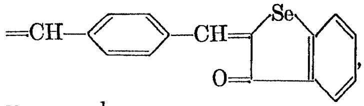
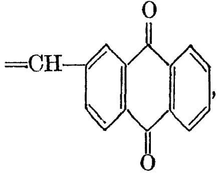
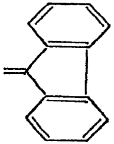
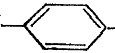
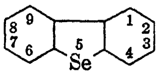
Substituent	M.p., °C.	Ref.	Deriv.	M p., °C.	Ref.
3-Hydroxy (*contd*)...............			2-Furylidene, orange	145–147	247
			2-(*p*-Nitrobenzylidene), red-golden	243–244	247
			2-(2,4-Dinitrobenzylidene), red and orange form	226–227 (dec.)	247
			2-(*o*-Formylbenzylidene), brown-yellow	206–207	247
			2-(*o*-Carboxybenzylidene), yellow	226–227	247
			2-(α-Naphthylidene), red	244–245	247
			2-(β-Naphthylidene), light red	210–211	247
			2-(β-Methoxy-α-naphthylidene), yellow	127–128	247
			2- , orange-red	330 Subl. 290	247
			2- , orange-red	348–349 Subl. 270	247

Table continued

TABLE IX-1 (*continued*)

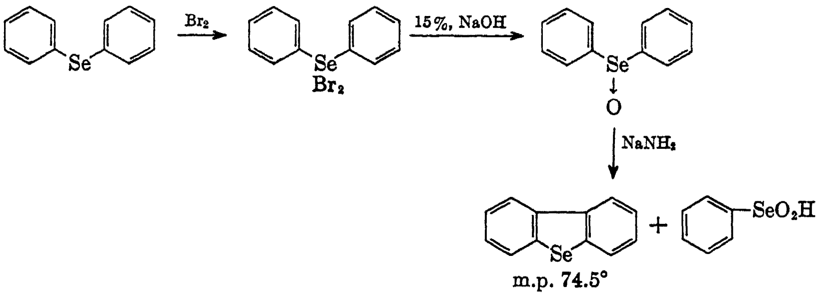
Substituent	M.p., °C.	Ref.	Deriv.	M.p., °C.	Ref.
3-Hydroxy (*contd.*)			2- 	169–171	247
			3-Semicarbazone	245	330
2,3-Quinone	102–103 Subl. 100	8,441	Picrate	120	330
			3-Anil, yellow	218–219	348
			3- =N—  —N(CH$_3$)$_2$, granite red	226 (dec.)	348
			2-imide, grey	235	441
Di-(2-amino-3-hydroxy)sulfate	120 (dec.)	441			
2-Bromo-3-hydroxy	103	348,441			
3,6-Di-CH$_3$-4,7-di-OH	152	614			
3,6-Di-CH$_3$-4,5,7-tri-OH	188 (dec.)	614			
3,6-Di-CH$_3$-4,7-quinone	138	614	Monoxime, yellow	215	614
			2,4-Dinitrophenylhydrazone	269 (dec.)	614
2,5-Di-Br-3,6-di-CH$_3$-4,7-quinone	Not listed	614			
3,6-Di-CH$_3$-5-OH-4,7-quinone	189	614	5-CH$_3$O, ochre	124	614
			5-CH$_3$COO, yellow	167	614

C. Dibenzoselenophene



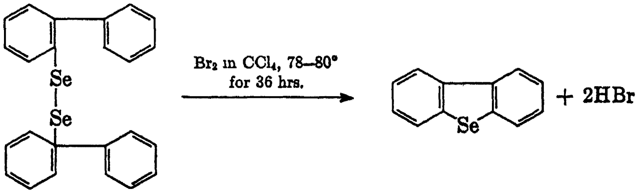
(*Ring Index* No. 1748)

Dibenzoselenophene was first prepared in 1934 by Courtot and Matamedi (128) by a synthesis originally employed for dibenzothiophene. The synthesis involves the ring closure of diphenyl selenoxide in the presence of sodamide. Equation 12 outlines the synthesis from diphenyl selenide.



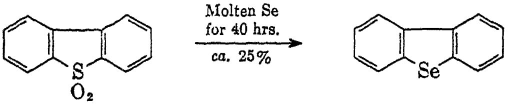
(12)

The more recent method developed by McCullough, Campbell, and Gould (653) appears to be the best preparative method from the standpoint of intermediates and yield. This method involves the simple bromination of di-(*o*-diphenylyl)diselenide. The ring closure appears to be due to the formation of an unstable *o*-diphenylselenium bromide which loses hydrogen bromide (eq. 13). This modification is a considerable improvement of an old method in which *o*-diphenylselenium trichloride or tribromide was isolated and then heated with 25% alcoholic KOH to effect ring closure (38).

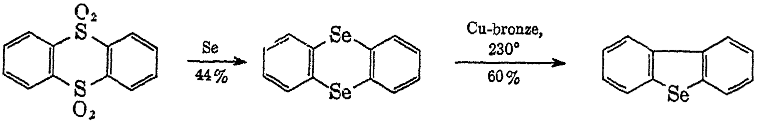


(13)

Another type of synthesis involves replacing the sulfur of dibenzothiophene 5-dioxide (137) or thianthrene 5,10-tetraoxide (139) by selenium



(14)

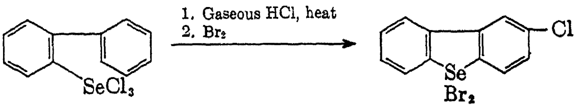


(15)

(eqs. 14 and 15). These syntheses were originally developed for the preparation of dibenzothiophene.

When *o*-aminodiphenyl selenide is diazotized and heated, only a trace of dibenzoselenophene is obtained (139). This same method with *o*-aminodiphenyl sulfide affords respectable yields of dibenzothiophene.

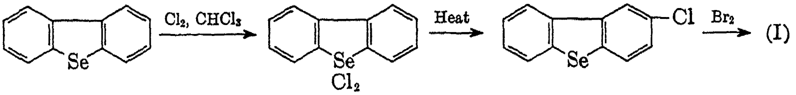
When *o*-diphenylselenium trichloride is heated in a solvent in a stream of hydrogen chloride, 5,5-dichlorodibenzoselenophene, m.p. 136–137°, is obtained. Without a solvent, a colorless product is obtained which when treated with bromine gives a product said to be 2-chloro-5,5-dibromodibenzoselenophene (I), m.p. 130–131° (38) (eq. 16).



(I)

(16)

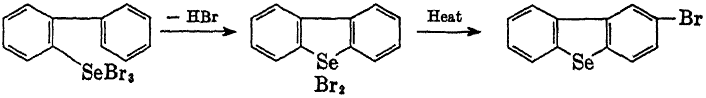
This material has also been made by the following series of reactions:



(17)

m.p. 136–137° Liquid m.p. 130–131°

The *o*-diphenylselenium tribromide when heated at its melting point yields 2-bromodibenzoselenophene (38). Apparently this compound is formed by thermal decomposition of the intermediate 5,5-dibromide, since it was later found that the latter material yielded the same compound (39) (eq. 18). The structure of 5,5-dichlorodibenzoselenophene was indicated



(18)

m.p. 129° m.p. 95–96°

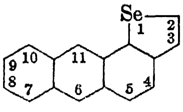
by conversion to the 5-oxide (39). Sodium hydroxide solution (3%) gives the same product, while 15% sodium hydroxide solution gives a mixture of the 5-oxide and dibenzoselenophene (128). 5,5-Dibromodibenzoselenophene is formed by the action of bromine on dibenzoselenophene (128,39). Its melting point (with decomposition) is reported to be 121.5° (128) and 129° (39).

No direct substitution reactions of the benzenoid rings have been undertaken other than by the rearrangements of the 5,5-dihalo derivatives described above. Substitution in this case was assumed to take place in the 2-position. Direct oxidation of dibenzoselenophene with peracetic acid in acetic acid gives dibenzoselenophene 5-oxide, m.p. 229–230°, in 48% yield (653). The same compound obtained from hydrolysis of the 5-dichloro derivatives (39) melted at 219–221° (dec.). Gould and McCullough (726) report that the 5-oxide forms 1:1 complexes with mercuric chloride (m.p. 182° dec.), mercuric bromide (m.p. 191° dec.), and mercuric iodide (m.p. 218° dec.). The 5-dioxide of dibenzoselenophene (m.p. 282°) results from direct oxidation of the 5-oxide with potassium permanganate (128).

Note added in proof: Sawicki and Ray (773) have recently announced the mononitration of dibenzoselenophene and subsequent reduction of this compound to the monoamine. From a comparison of the ultraviolet absorption curves of these derivatives with those of the corresponding 2-derivatives of dibenzothiophene, it was concluded that dibenzoselenophene substituted in the 2-position. Buu-Hoï and Hoán also have presented evidence for 2-substitution (774). These authors also reported that the Friedel and Crafts reaction, the Beckmann rearrangement and the Pfitzinger reaction take place in this series with the same ease as in the dibenzothiophene series (775). The original literature (773–775) should be consulted for the physical constants of the new derivatives and the several new condensed selenophene ring systems reported.

Dibenzoselenophene dissolves in concentrated sulfuric acid to produce a deep-blue color which becomes purple on warming. The dipole moment ($\mu \times 10^{-18}$) is 0.41 (706).

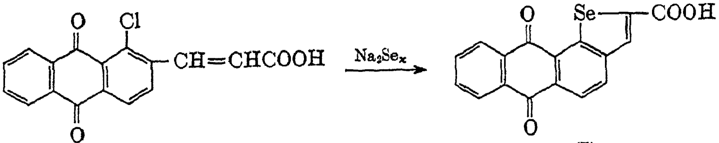
D. Anthraselenophene



(*Ring Index* No. 2510)

Anthra[1,2-*b*]selenophene derivatives are formed by treatment of 1-chloroanthraquinone-2-acrylic acid with sodium polyselenide, and 6,11-

dioxo-2-anthra[1,2-*b*]selenophenecarboxylic acid (I) results (288, P-578) (eq. 19). The orange-colored compound (I) can be vatted to produce a



(19)

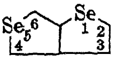
(I)
m.p. 347–349° (dec.)

deep wine-colored vat. It can also be decarboxylated to yield bronze-colored 6,11-anthra[1,2-*b*]selenophenequinone, m.p. 213.5–214.5°. When methylated by means of the Grignard reaction, 6,11-dimethylanthra[1,2-*b*]-selenophene is formed. This yellow compound melts at 118–118.5°, it forms a picrate, m.p. 145–146°, and a trinitrobenzene complex, m.p. 173.5–174°.

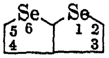
II. Heterocyclic Condensed Selenophene Systems

A. The Isomeric Selenophthenes

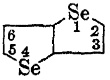
Umezawa and collaborators have studied the residues obtained in the preparation of selenophene from acetylene and selenium (631,632). These were found to contain selenopheno[3,4-*b*]selenophene (I), selenopheno[2,3-*b*]selenophene (II), and selenopheno[3,2-*b*]selenophene (III), as well as selenonaphthene (IV).



(I)



(II)



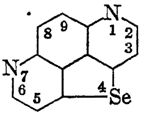
(III)

The structures of the materials were assigned from a study of dipole moments. I has a dipole moment, $\mu \times 10^{-18}$, of 1.07, II, 1.52, and III, zero. In addition, I has a magnetic susceptibility, $-\chi_m \times 10^6$, of 110–111, while the susceptibility of III is only 70–77 (664).

Separation of the isomers was carried out in the following manner. I crystallizes from the acetylene-selenium residues after standing for one month. It melts at 123–124.5°; II is obtained as an oil, b.p. 93° (14 mm.), d_4^{25} 1.9354, n_D^{25} 1.6586, by steam distillation of the filtrate from I. III is not readily volatile with steam and is vacuum distilled from the residues. It melts at 51–51.5°. Only the I and III isomers form picrates (picrate of I, m.p. 163–165°; picrate of III, m.p. 154–155.5°). All three isomers form tetrabromo derivatives with bromine [tetrabromo (I), m.p. 246–247.4°; tetrabromo (II), m.p. 271–272°; tetrabromo (III), m.p. 252–253°].

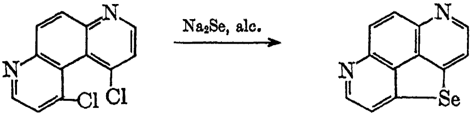
Umezawa in his later article (632) referred to I as selenopheno[2,3-*b*] selenophene, but *Chemical Abstracts* made no further reference to the inversion of formula I and II. In this instance, Umezawa (632) nitrated the isomer referred to as selenopheno[2,3-*b*]selenophene (this is isomer I according to the first article) (631). He obtained a mononitro derivative (m.p. 108–109.5°) with acetyl nitrate. With sulfuric acid, this isomer yielded a disulfonic acid that was isolated through the dibarium salt and subsequently converted to a disulfonyl chloride (m.p. 234–236°) with phosphorus pentachloride.

B. Seleno[*lmn*] [4,7]phenanthroline



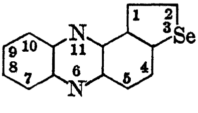
(*Ring Index* No. 2509)

The patent literature describes the preparation of seleno[*lmn*][4,7]phenanthroline from the condensation of sodium selenide and 1,10-dichloro-4,7-phenanthroline (P-251,P-580) (eq. 20). 3,8-Dimethyl-1,10-dichloro-4,7-phenanthroline is cyclized to 2,6-dimethylseleno[*lmn*][4,7]phenanthroline, m.p. 232° by the above method. These two compounds can also be prepared by warming selenourea with the dichlorophenanthrolines. Hydrogen chloride is evolved in the reaction.



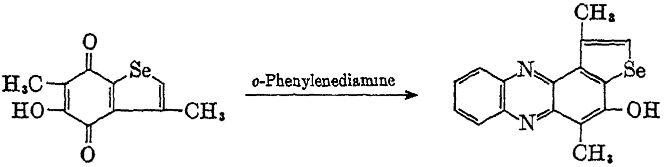
(20)

C. Selenonaphtheno [4,5-*b*]quinoxaline



Selenonaphtheno [4,5-*b*] quinoxaline

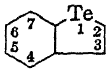
A derivative of this ring system results when 3,6-dimethyl-5-hydroxy-4,7-selenonaphthenequinone is reacted with *o*-phenylenediamine (614) (eq. 21). This compound is reported to sublime at 250°.



(21)

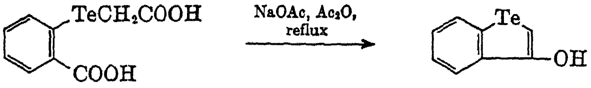
III. Condensed Tellurophene Systems

A. Telluronaphthene



(*Ring Index* No. 857)

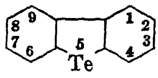
Telluronaphthene has not been prepared. The only derivative of this series known is 3-hydroxytelluronaphthene. It has been synthesized by the ring-closure methods applied in the thianaphthene series (380) (eq. 22).



(22)

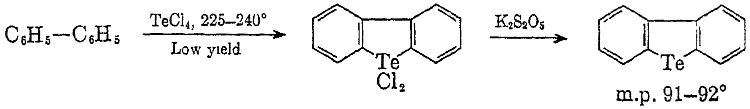
3-Hydroxytelluronaphthene is reported to melt at 200°, but begins decomposing at 160°. It is a yellowish white powder. It does not oxidize to the corresponding telluroindigo. Whether this indicates that the compound does not exist in the keto form or whether oxidation takes place at the tellurium atom was not reported.

B. Dibenzotellurophene



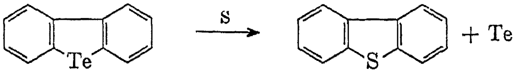
(*Ring Index* No. 1749)

Dibenzotellurophene has been prepared from diphenyl and tellurium tetrachloride or tetrabromide via an intermediate 5,5-dichloro derivative (129) (eq. 23). 5,5-Dibromodibenzotellurophene, m.p. 210–220° (dec.)

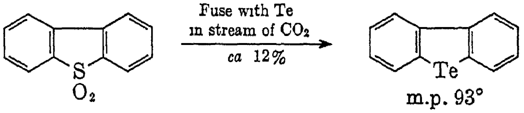


(23)

prepared by the action of tellurium tetrabromide on diphenyl, decomposes on melting to yield 4,4′-dibromodiphenyl (129). 5,5-Dichlorodibenzotellurophene is reported to decompose at 200° to yield dibenzotellurophene 5-oxide. The latter compound is reconverted to the 5.5-dihalogen derivative by means of hydrochloric acid. Dibenzotellurophene when warmed with sulfur yields dibenzothiophene (eq. 24). Displacement of the —SO_2— in dibenzothiophene 5-dioxide by tellurium has been carried out to yield dibenzotellurophene (139) (eq. 25). Dibenzotellurophene is reported to be a colorless solid dissolving in concentrated sulfuric acid to give a violet color which reverts to a colorless state on standing (139).



(24)



(25)

BIBLIOGRAPHY

1. Adickes and Krawczyk, *Ber.*, *B74*, 1389 (1941).
2. Alder, Rickert, and Windemuth, *Ber.*, *B71*, 2451 (1938).
3. Allen and Gates, *J. Am. Chem. Soc.*, *65*, 1283 (1943).
4. Alt, *Farberztg.*, *17*, 169 (1906); *Centr.*, *1906*, II, 286.
5. Amick, *Chem. Age*, *21*, No. 533, *Dyestuffs Monthly Suppl. 21* (1929); *Centr.*, *1930*, I, 590.
6. Ancizar-Sordo and Bistrzycki, *Helv. Chim. Acta*, *14*, 141 (1931).
7. Angelico, *Gazz. chim. ital.*, *41*, *II*, 378 (1911); *Chem. Abstracts*, *6*, 353 (1912)
8. Anker and Cook, *J. Chem. Soc.*, *1944*, 489.
9. Anon., *Rev. gén. mat. color.*, *18*, 110 (1914); *Chem. Abstracts*, *8*, 2950 (1914).
10. Appleton and Geake, *Trans. Faraday Soc.*, *37*, 45 (1941).
11. Apitzsch, *Ber.*, *41*, 4047 (1908).
12. Apitzsch and Kelber, *Ber.*, *43*, 1259 (1910).
13. Apitzsch, *Ber.*, *46*, 3091 (1913).
14. Arndt, Kirsch, and Nachtweg, *Ber.*, *B59*, 1074 (1926).
15. Arndt and Pusch, *Ber.*, *B59*, 1646 (1925).
16. Arndt and Martius, *Ann.*, *499*, 228 (1932).
17. Asahina and Tukamoto, *Ber.*, *B71*, 308 (1938).
18. Auwers and Arndt, *Ber.*, *42*, 537 (1909).
19. Auwers and Müller, *Ann.*, *381*, 276 (1911).
20. Auwers, *Ann.*, *393*, 338 (1912).
21. Auwers, *Ber.*, *45*, 994 (1912).
22. Auwers, Boennecke, Krollpfeiffer, and Peter, *Ann.*, *408*, 212 (1915).
23. Auwers and Thies, *Ber.*, *B53*, 2285 (1920).
24. Auwers and Kohlhass, *J. prakt. Chem.*, *108*, 321 (1924).
25. Auwers and Susemihl, *Z. physik. Chem.*, *A148*, 125 (1930); *Chem. Abstracts*, *24*, 5233 (1930).
26. Auwers, *Ber.*, *B65*, 831 (1932).
27. Avakian, Moss, and Martin, *J. Am. Chem. Soc.*, *70*, 3075 (1948); see also Avakian and Martin, U. S. Pat. 2,517,826 (1940).
28. Backer, Strating, and Huisman, *Rec. trav. chim.*, *60*, 381 (1941).
29. Backer and van der Bij, *Rec. trav. chim.*, *62*, 561 (1943).
30. Barber and Smiles, *J. Chem. Soc.*, *1928*, 1141.
31. Barchewitz and Garach, *Compt. rend.*, *208*, 2071 (1939).
32. Barger and Ewins, *J. Chem. Soc.*, *93*, 2086 (1908).
33. Barry and McClelland, *J. Chem. Soc.*, *1935*, 471.
34. Bartlett and McClelland, *J. Chem. Soc.*, *1934*, 818.
35. Barton and McClelland, *J. Chem. Soc.*, *1947*, 1574.
36. Baumann, *Bull. Soc. Ind. Mulhouse*, *94*, 372 (1928); *Centr.*, *1928*, II, 1152.
37. Bechamp, *Compt. rend.*, *148*, 1677 (1909).
38. Behaghel and Hofmann, *Ber.*, *B72*, 582 (1939).
39. Behaghel and Hofmann, *Ber.*, *B72*, 697 (1939).
40. Bellavita, *Gazz. chim. ital.*, *70*, 594 (1940); *Chem. Abstracts*, *35*, 1405 (1941).
41. Benary and Bavarian, *Ber.*, *48*, 593 (1915).
42. Benary, *Ber.*, *51*, 572 (1918).
43. Bennett and Hafez, *J. Chem. Soc.*, *1941*, 287.
44. Bennett and Hafez, *J. Chem. Soc.*, *1941*, 652.
45. Bergmann and Tschudnowsky, *Z. physik. Chem.*, *B17*, 107 (1932); *Centr.*, *1932*, II, 28.
46. Bezdrik, Friedländer, and Koeniger, *Ber.*, *41*, 227 (1908).
47. Bezdrik and Friedländer, *Monatsh.*, *29*, 375 (1908).

48. Bezzubets and Ignatyuk-Maĭstrenko, *J. Chem. Ind. (U.S.S.R.)*, *18*, No. 10, 16 (1941); *Chem. Abstracts*, *38*, 3477 (1944).
49. Biedermann, *Ber.*, *19*, 1615 (1886).
50. Bistrzycki and Traub, *Helv. Chim. Acta*, *7*, 935 (1924).
51. Bistrzycki and Risi, *Helv. Chim. Acta*, *8*, 582 (1925).
51a. Blicke and Sheets, *J. Am. Chem. Soc.*, *70*, 3768 (1948).
52. Blicke and Sheets, *J. Am. Chem. Soc.*, *71*, 2856 (1949).
53. Blicke and Sheets, *J. Am. Chem. Soc.*, *71*, 4010 (1949).
54. Block, Lehr, and Erlenmeyer, *Helv. Chim. Acta*, *28*, 1406 (1945)
55. Boes, *Apothekerztg.*, *17*, 565 (1902); *Centr.*, *1902*, II, 804.
56. Bohm, *Hoppe-Seyler's Z. physiol. Chem.*, *269*, 17 (1941), *Centr.*, *1942*, I, 1527.
57. Bolt and Backer, *Rec. trav. chim.*, *55*, 898 (1936).
58. Bonino and Manzoni-Ansidei, *Mem. acad. sci. inst Bologna, classe sci. fis.* (9), *1*, Sep. (Feb. 18, 1934); *Chem. Abstracts*, *29*, 1712 (1935)
59. Bordwell and Albisetti, *J. Am. Chem. Soc.*, *70*, 1558 (1948).
60. Bordwell and Albisetti, *J. Am. Chem. Soc.*, *70*, 1955 (1948).
61. Bordwell, Lampert, and McKellin, *J. Am. Chem Soc.*, *71*, 1702 (1949).
62. Bordwell *et al.*, to be published.
63. Borsche and R. Meyer, *Ber.*, *54*, 2854 (1921).
64. Brass and Köhler, *Ber.*, *B55*, 2543 (1922).
65. Brass and Mosl, *Ber.*, *B59*, 1266 (1926).
66. Brass and Torinus, *Kolloid-Z.*, *45*, 256 (1928); *Centr.*, *1928*, II, 1037.
67. von Braun, *Ber.*, *B58*, 2165 (1925).
68. von Braun and Weissbach, *Ber.*, *B62*, 2416 (1929).
69. Brown, Christiansen, and Sandin, *J. Am. Chem. Soc.*, *70*, 1748 (1948).
70. Bruson and Kroeger, *J Am. Chem. Soc.*, *62*, 36 (1940).
71. Burger, Wartman, and Lutz, *J. Am. Chem. Soc.*, *60*, 2628 (1938).
72. Burger and Bryant, *J. Org. Chem.*, *4*, 119 (1939).
73. Burger and Bryant, *J. Am. Chem. Soc.*, *63*, 1054 (1941).
74. Burtner and Lehmann, *J. Am. Chem. Soc.*, *62*, 527 (1940).
75. Bushland and King, *U.S. Dept. of Agr., Bur. Entomol. Plant Quarantine E-585*, 15 pp. (1943); *Chem. Abstracts*, *37*, 2111 (1943).
76. Buu-Hoï and Cagniant, *Rec. trav. chim.*, *62*, 719 (1943).
77. Buu-Hoï and Cagniant, *Ber.*, *B76*, 1269 (1943).
78. Buu-Hoï and Lecocq, *Compt. rend.*, *222*, 1441 (1946).
79. Buu-Hoï and Royer, *Compt. rend.*, *223*, 806 (1946).
80. Buu-Hoi and Cagniant, *Bull. soc. chim. France*, *1946*, 123.
81. Buu-Hoï and Nguyen-Hoan, *Rec. trav. chim.*, *67*, 309 (1948).
82. Buu-Hoï and Cagniant, *Rec. trav. chim.*, *67*, 64 (1948).
83. Buu-Hoï and Royer, *Rec. trav. chim.*, *67*, 175 (1948).
84. Buu-Hoï Hoan, Khôi, and Xuong, *J. Org. Chem.*, *14*, 802 (1949).
85. Buu-Hoï and Nguyen-Hoán, *Rec. trav. chim.*, *68*, 5 (1949).
86. Buu-Hoï and Nguyen-Hoán, *Rec. trav. chim.*, *68*, 441 (1949).
87. Buu-Hoï *et al.*, *Rec. trav. chim.*, *68*, 473 (1949).
88. Bistrzycki and Brenken, *Helv. Chim. Acta*, *5*, 20 (1922).
89. Cagniant and Deluzarche, *Compt. rend.*, *222*, 1301 (1946).
90. Cagniant, *Bull. soc. chim. France*, *1949*, 382.
91. Cândea, *Bull. sci. école polytech. Timisoara*, *8*, 191 (1939); *Chem. Abstracts*, *33*, 4986 (1939).
92. Chaix, *Bull. soc. chim. France*, *53*, 700 (1933).
93. Chaix, *Compt. rend.*, *200*, 1208 (1935).
94. Chaix and Rochebouët, *Bull. soc. chim. France*, (5), *2*, 273 (1935).
95. Chaix and Fromageot, *Enzymologia*, *1*, 321 (1937); *Chem. Abstracts*, *31*, 5006 (1937).

96. Chakravarti, *J. Indian Chem. Soc.*, *5*, 405 (1928); *Chem. Abstracts*, *23*, 127 (1929).
97. Challenger, *J. Soc. Chem. Ind.*, *48*, 622 (1929).
98. Challenger and Gibson, *J. Inst. Pet. Tech.*, *21*, 135 (1935).
99. Challenger and Miller, *J. Chem. Soc.*, *1939*, 1005.
100. Challenger and Clapham, *J. Chem. Soc.*, *1948*, 1615.
101. Chandra, Chakrabarty, and Mitra, *J. Indian Chem. Soc.*, *19*, 139 (1942).
102. Charlampowicz and Marchlewski, *Bull. intern. acad. polonaise*, *A1930*, *376; Chem. Abstracts*, *25*, 5097 (1931).
103. Charles and Freiser, *J. Am. Chem. Soc.*, *72*, 2233 (1950).
104. Cheney and Piening, *J. Am. Chem. Soc.*, *67*, 2252 (1945).
105. Chilikin, *J. Russ. Phys. Chem. Soc.*, *47*, 539 (1915); *Chem. Abstracts*, *9*, 2507 (1915).
106. Chilikin, *Ber.*, *B65*, 1651 (1932).
107. Chilikin and Karpowa, *Centr.*, *1932*, II, 1299.
108. Chmelewski and Friedländer, *Ber.*, *46*, 1903 (1913).
109. Chovin, *Bull. soc. chim.*, *11*, 82 (1944).
110. Chovin, *Bull. soc. chim.*, *11*, 91 (1944).
111. Claaz, *Ber.*, *49*, 2079 (1916).
112. Clapp, *J. Am. Chem. Soc.*, *61*, 2733 (1939).
113. Clibbens and Little, *J. Textile Inst.*, *37*, T219 (1946); *Chem. Abstracts*, *41*, 1844 (1947).
114. Cohen and Smiles, *J. Chem. Soc.*, *1930*, 406.
115. Colonna, *Gazz. chim. ital.*, *70*, 154 (1940); *Chem. Abstracts*, *34*, 4737 (1940).
116. Corbellini and Albenga, *Gazz. chim. ital.*, *61*, 111 (1931); *Chem. Abstracts*, *25*, 3340 (1931).
117. Courtot and Pomonis, *Compt. rend.*, *182*, 893 (1926).
118. Courtot and Pomonis, *Compt. rend.*, *182*, 931 (1926).
119. Courtot, Nicolas, and Tchang, *Compt. rend.*, *186*, 1624 (1928).
120. Courtot and Evain, *Bull. soc. chim. France*, *49*, 527 (1931).
121. Courtot and Evain, *Bull. soc. chim. France*, *49*, 1555 (1931).
122. Courtot and Chaix, *Compt. rend.*, *192*, 1667 (1931).
123. Courtot and Lin, *Bull. soc. chim. France*, *49*, 1047 (1931).
124. Courtot, Chaix, and Kelner, *Compt. rend.*, *194*, 1837 (1932).
125. Courtot, Chaix, and Nicolas, *Compt. rend.*, *194*, 1660 (1932).
126. Courtot and Kelner, *Compt. rend.*, *198*, 2003 (1934).
127. Courtot, *Compt. rend.*, *198*, 2260 (1934).
128. Courtot and Motamedi, *Compt. rend.*, *199*, 531 (1934).
129. Courtot and Bastani, *Compt. rend.*, *203*, 197 (1936).
130. Cox, Gillot, and Jeffrey, *Acta Crystallog.*, *2*, 356 (1949); *3*, 243 (1950).
131. Craik and MacBeth, *J. Chem. Soc.*, *127*, 1637 (1925).
132. Crook, Davies, and Smith, *Nature*, *139*, 154 (1937).
133. Crook and Davies, *J. Chem. Soc.*, *1937*, 1697.
134. Cullinane and Padfield, *J. Chem. Soc.*, *1935*, 1131.
134a. Cullinane, *J. Chem. Soc.*, *1932*, 2365.
135. Cullinane, C. Davies, and G. Davies, *J. Chem. Soc.*, *1936*, 1435.
136. Cullinane and Davies, *Rec. trav. chim.*, *55*, 881 (1936).
137. Cullinane, Morgan, and Plummer, *Rec. trav. chim.*, *56*, 627 (1937)
138. Cullinane and Plummer, *J. Chem. Soc.*, *1938*, 63.
139. Cullinane, Rees, and Plummer, *J. Chem. Soc.*, *1939*, 151.
140. Dalgliesh and Mann, *J. Chem. Soc.*, *1945*, 893.
140a. Dalgliesh and Mann, *J. Chem. Soc.*, *1945*, 910.
140b. Dalgliesh and Mann, *J. Chem. Soc.*, *1945*, 913.
141. Dalgliesh and Mann, *J. Chem. Soc.*, *1947*, 653.

142. Dănăilă and Cândea, *Bull. sect. sci. acad. roumaine*, *4*, 334 (1916); *Chem. Abstracts.* *10*, 2095 (1916).
143. Danaila, *Bull. soc. chim. France*, (4), *7*, 359 (1910).
144. Denison and Condit, *Ind. Eng. Chem.*, *37*, 1102 (1945).
145. Déribéré, *Tiba*, *15*, 349 (1937); *Chem. Abstracts*, *32*, 1602 (1938)
146. Dilthey, Graef, Diericks, and Josten, *J. prakt. Chem.*, *151*, 185 (1938); *Chem Abstracts*, *33*, 579 (1939).
147. Dokunikhin and Levin, *Compt. rend. acad. sci., U.R.S.S.*, *35*, 110 (1942); *Chem. Abstracts*, *37*, 1929 (1943).
148. Donzelot and Chaix, *Compt. rend.*, *202*, 851 (1936).
149. D'Silva and McClelland, *J. Chem. Soc.*, *1932*, 2883.
150. Dudley, Bronson, and Harris, *U.S. Dept. of Agr., Bur. Entomol. Plant Quarantine* E-651, 10 pp. (1945); *Chem. Abstracts*, *39*, 3111 (1945).
151. Dufraisse and Daniel, *Bull. soc. chim. France*, (5), *4*, 2063 (1937).
152. Dunlap and Warren, *Cancer Research*, *1*, 953 (1941); *Chem. Abstracts*, *36*, 1082 (1942).
153. Dutt, *J. Chem. Soc.*, *1926*, 1171.
154. Dutta, *J. Indian Chem. Soc.*, *9*, 99 (1932); *Chem. Abstracts*, *26*, 4047 (1932).
155. Dutta, *Ber.*, *B66*, 1223 (1933).
156. Dutta, *Ber.*, *B66*, 1226 (1933).
157. Dutta, *Ber.*, *B66*, 1230 (1933).
158. Dutta, *Ber.*, *B67*, 5 (1934).
159. Dutta, *Ber.*, *B67*, 9 (1934).
160. Dutta, *Ber.*, *B67*, 1319 (1934).
161. Dutta, *Ber.*, *B67*, 1324 (1934).
162. Dutta, *Ber.*, *B68*, 1447 (1935).
163. Dutta, *Ber.*, *B69*, 2343 (1936).
164. Dutta, *J. Indian Chem. Soc.*, *18*, 469 (1941); *Chem. Abstracts*, *36*, 4505 (1942).
165. Dutta and Sinha, *J. Indian Chem. Soc.*, *18*, 477 (1941); *Chem. Abstracts*, *36*, 4505 (1942).
166. Dutta and Sinha, *J. Indian Chem. Soc.*, *19*, 239 (1942); *Chem. Abstracts*, *37*, 1873 (1943).
167. Dutta, *J. Indian Chem. Soc.*, *26*, 27 (1949); *Chem. Abstracts*, *44*, 331 (1950).
168. Dziewonski and Bachman, *Ber.*, *36*, 962 (1903).
169. Dziewonski and Prokopczuk, *Chem. Abstracts*, *18*, 983 (1924).
170. Dziewonski and Rychlik, *Ber.*, *B58*, 2239 (1925).
171. Dziewonski, Baraniecki, and Sternbach, *Bull. intern. acad. polonaise*, *A1930*, 198; *Chem. Abstracts*, *25*, 5292 (1931).
172. Dziewonski and Piasecki, *Bull. intern. acad. polon.*, *A1932*, 287; *Chem. Abstracts*, *28*, 2349 (1934).
173. Dziewonski and Sternbach, *Roczniki Chem.*, *17*, 101 (1937); *Chem. Abstracts*, *31*, 4976 (1937).
174. Dziewonski and Marusinska, *Bull. intern. acad. polon sci., Classe sci. math. nat.*, *A1938*, 316; *Chem. Abstracts*, *33*, 1712 (1939).
175. Eibner, *Chem. Ztg.*, *32*, 1032 (1909); *Centr.*, *1909*, I, 1364.
176. Elliott and Harington, *J. Chem. Soc.*, *1949*, 1374.
177. Emerson, Holly, and Klemm, *J. Am. Chem. Soc.*, *63*, 2569 (1941).
178. Erban, *Farbenzeitung*, *17*, 138 (1906); *Centr. 1906*, I, 1855.
179. Etienne, *Bull. soc. chim. France*, *1947*, 634.
180. Evans and DeHeer, *Acta Crystallog.*, *2*, 363 (1949).
181. Feist, Pauschardt, and Dibbern, *Ber.*, *B58*, 2311 (1925).
182. Felix and Friedländer, *Monatsh.*, *31*, 55 (1910).
183. Fieser and Ames, *J. Am. Chem. Soc.*, *49*, 2604 (1927).
184. Fieser and Kennelly, *J. Am. Chem. Soc.*, *57*, 1611 (1935).

185 Fieser and Desreux, *J. Am. Chem. Soc.*, *60*, 2255 (1938).
186. Finger and Eirich, *J. prakt. Chem.*, *103*, 249 (1921); *Chem. Abstracts*, *16*, 1413 (1922).
187. Fink and Smith, *J. Econ. Entomol.*, *29*, 804 (1936); *Chem. Abstracts*, *30*, 7722 (1936).
188. Flowers and Flowers, *J. Am. Chem. Soc.*, *71*, 3102 (1949) and U.S. Pat. 2,499,186 (1950).
189. Formanek, *Chem. obzor*, *3*, 133 (1928); *Chem. Abstracts*, *22*, 3583 (1928).
190. Fowkes and McClelland, *J. Chem. Soc.*, *1941*, 187.
191. Fowkes and McClelland, *J. Chem. Soc.*, *1945*, 405.
192. Fricke and Spilker, *Ber.*, *B58*, 24 (1925).
193. Fricke and Spilker, *Ber.*, *B58*, 1589 (1925).
194. Fricke and Spilker, *Ber.*, *B59*, 349 (1926).
195. Friedländer, *Ber.*, *39*, 1060 (1906).
196. Friedländer, *Z. angew. Chem.*, *19*, 615 (1906); *Centr.*, *1906*, I, 1581.
197. Friedländer, *Ann.*, *351*, 390 (1907).
198. Friedländer, *Ber.*, *41*, 772 (1908).
199. Friedländer, *Monatsh.*, *29*, 359 (1908).
199a. Friedländer, *Monatsh.*, *29*, 375 (1908).
200. Friedlander, *Ber.*, *41*, 1035 (1908).
201. Friedländer, *Ber.*, *42*, 1058 (1909); see also Ger. Pat. 193,272.
202. Friedländer, *Monatsh.*, *30*, 347 (1907).
203. Friedländer and Schwenk, *Ber.*, *43*, 1971 (1910).
204. Friedländer and Kielbasinski, *Ber.*, *44*, 3098 (1911)
205. Friedländer and Woroshzow, *Ann.*, *388*, 1 (1912).
206. Friedländer and Lenk, *Ber.*, *45*, 2083 (1912).
207. Friedländer and Risse, *Ber.*, *47*, 1919 (1914).
208. Friedländer, *Ber.*, *49*, 955 (1916).
209. Friedländer, Herzog, and Voss, *Ber.*, *55*, 1591 (1922).
210. Friedländer and Kunz, *Ber.*, *55*, 1597 (1922).
211. Friedlander and Sander, *Ber.*, *B57*, 637 (1924).
212. Friedländer and Sander, *Ber.*, *B57*, 648 (1924).
213. Friedländer, *Ann.*, *443*, 211 (1925).
214. Friedmann, *Ber.*, *49*, 50 (1916).
215. Fries and Finck, *Ber.*, *41*, 4284 (1908).
216. Fries and Bartholomäus, *Ann.*, *405*, 373 (1914).
217. Fries and Schürmann, *Ber.*, *B52*, 2170 (1919).
218. Fries and Ehlers, *Ber.*, *B56*, 1308 (1923).
219. Fries, Koch, and Stukenbrock, *Ann.*, *468*, 162 (1929).
220. Fries and Hemmecke, *Ann.*, *470*, 1 (1929).
221. Fries, Franke, and Bruns, *Ann.*, *511*, 241 (1934).
222. Fries, Heering, Hemmecke, and Siebert, *Ann.*, *527*, 83 (1937).
223. Fuchs, *Monatsh.*, *53*, *54*, 438 (1929).
224. Fuchs and Gross, *Ber.*, *63*, 1013 (1930).
225. Fürst and Pollak, *Ber.*, *B65*, 390 (1932).
226. Gattermann and Lockhardt, *Ber.*, *26*, 2808 (1893).
227. Gattermann, *Ann.*, *393*, 113 (1912).
228. Gebauer-Fülnegg and Jarsch, *Monatsh.*, *56*, 317 (1930).
229. Gerhardt, *Monatsh.*, *42*, 63 (1921).
230. Ghosh, *J. Indian Chem. Soc.*, *14*, 713 (1937); *Chem. Abstracts*, *32*, 4166 (1938).
231. Gilman and Jacoby, *J. Org. Chem.*, *3*, 108 (1938).
232. Gilman, Jacoby, and Pacevitz, *J. Org. Chem.*, *3*, 120 (1938).
233. Gilman and Bebb, *J. Am. Chem. Soc.*, *61*, 109 (1938).
234. Gilman *et al.*, *J. Am. Chem. Soc.*, *62*, 2606 (1940).
235. Gilman, Moore, and Baine, *J. Am. Chem. Soc.*, *63*, 2479 (1941).

236. Gilman, Meals, O'Donnell, and Woods, *J. Am. Chem. Soc*., *65*, 268 (1943).
237. Gilman and Stuckwisch, *J. Am. Chem. Soc.*, *67*, 877 (1945).
238. Gilman, Haubein, O'Donnell, and Woods, *J. Am. Chem. Soc.*, *67*, 922 (1945).
239. Gilman and Nobis, *J. Am. Chem. Soc.*, *67*, 1479 (1945).
240. Gilman and Avakian, *J. Am. Chem. Soc.*, *68*, 1514 (1946).
241. Gilman and Avakian, *J. Am. Chem. Soc.*, *68*, 2104 (1946).
242. Gilman and Nobis, *J. Am. Chem. Soc.*, *71*, 274 (1949).
243. Gindraux, *Helv. Chim. Acta*, *12*, 931 (1929).
244. Godart, *J. chim. phys.*, *34*, 70 (1937).
245. Golosov, Gorlinskaya, and Rakklin, *Shertsyonoe Delo*, *16*, No. 4, 51 (1937); *Chem. Abstracts*, *33*, 4789 (1939).
246. Gössling, *Chem. Ind.*, *32*, 565 (1910); *Chem. Abstracts*, *5*, 383 (1911).
247. Graebe, *Ann.*, *174*, 185 (1874).
248. Graebe, *Ber.*, *7*, 50 (1874).
249. Grassmann and Arnim, *Ann.*, *519*, 192 (1935).
250. Griess and Duisberg, *Ber.*, *22*, 2467 (1889).
251. Griffith and Hope, *J. Chem. Soc.*, *127*, 990 (1925)
252. Grob, *Ber.*, *41*, 3331 (1908).
253. Grummitt and Helber, *J. Am. Chem. Soc.*, *63*, 3236 (1941).
253a. Guha, *J. Indian Chem. Soc.*, *9*, 423 (1932).
254. Guha, *J. Indian Chem. Soc.*, *10*, 679 (1933); *Chem. Abstracts*, *28*, 3905 (1934).
255. Guha and Basu-Mallick, *J. Indian Chem. Soc.*, *11*, 395 (1934); *Chem. Abstracts*, *28*, 6315 (1934).
256. Guha, *J. Indian Chem. Soc.*, *12*, 659 (1935); *Chem. Abstracts*, *30*, 1564 (1936).
257. Guha, *J. Indian Chem. Soc.*, *13*, 94 (1936); *Chem. Abstracts*, *30*, 4674 (1936).
258. Guha and Basu-Mallick, *J. Indian Chem. Soc.*, *13*, 571 (1936); *Chem. Abstracts*, *31*, 1618 (1937).
259. Guha, *J. Indian Chem. Soc.*, *14*, 240 (1937); *Chem. Abstracts*, *31*, 7253 (1937).
260. Guha, *J. Indian Chem. Soc.*, *14*, 709 (1937); *Chem. Abstracts*, *32*, 3966 (1938).
261. Guha, *J. Indian Chem. Soc.*, *15*, 20 (1938); *Chem. Abstracts*, *32*, 4787 (1938).
262. Guha, *J. Indian Chem. Soc.*, *15*, 359 (1938); *Chem. Abstracts*, *33*, 387 (1939).
263. Guha and Iyer, *J. Indian Inst. Sci.*, *A21*, 116 (1938); *Chem. Abstracts*, *33*, 2135 (1939); see also *Chem. Abstracts*, *43*, 2598 (1949).
264. Guha, *J. Indian Chem. Soc.*, *15*, 501 (1938); *Chem. Abstracts*, *33*, 2339 (1939).
265. Guha, *J. Indian Chem. Soc.*, *16*, 127 (1939); *Chem. Abstracts*, *33*, 9647 (1939).
266. Guha, *J. Indian Chem. Soc.*, *16*, 219 (1939); *Chem. Abstracts*, *33*, 7779 (1939).
267. Guha, *J. Indian Chem. Soc.*, *20*, 37 (1943); *Chem. Abstracts*, *37*, 6897 (1943).
268. Guha, *J. Indian Chem. Soc.*, *21*, 87 (1944); *Chem. Abstracts*, *39*, 1539 (1945).
269. Guha, *J. Indian Chem. Soc.*, *21*, 91 (1944); *Chem. Abstracts*, *39*, 1539 (1945).
270. Guha, *J. Indian Chem. Soc.*, *21*, 391 (1944); *Chem. Abstracts*, *39*, 4489 (1945).
271. Guha, *Bull. Patna Sci. Coll. Phil. Soc.*, No. *16*, 18 (1946); *Chem. Abstracts*, *40*, 5253 (1946).
272. Guha, *J. Indian Chem. Soc.*, *23*, 103 (1946); *Chem. Abstracts*, *40*, 6824 (1946).
273. Guha and Basu-Mallick, *J. Indian Chem. Soc.*, *23*, 214 (1946); *Chem. Abstracts*, *41*, 1843 (1947).
274. Guha and Chatterjee, *J. Indian Chem. Soc.*, *24*, 473 (1947); *Chem. Abstracts*, *42*, 8187 (1948).
275. Guha and Chatterjee, *J. Indian Chem. Soc.*, *25*, 429 (1948); *Chem. Abstracts*, *43*, 4855 (1949).
276. Gusev, *J. Applied Chem. (U.S.S.R.)*, *17*, 178 (1944); *Chem. Abstracts*, *39*, 1273 (1945).
277. Hamer, *J. Chem. Soc.*, *1939*, 1008.
278. Hansch and Lindwall, *J. Org. Chem.*, *10*, 381 (1945).
279. Hansch, *J. Am. Chem. Soc.*, *69*, 2908 (1947).

280. Hansch and Blondon, *J. Am. Chem. Soc.*, *70*, 1561 (1948).
281. Hansch and Hawthorne, *J. Am. Chem. Soc.*, *70*, 2495 (1948).
282. Harley-Mason and Mann, *J. Chem. Soc.*, *1942*, 404.
283. Hart and Smiles, *J. Chem. Soc.*, *125*, 876 (1924).
284. Hart, McClelland, and Fowkes, *J. Chem. Soc.*, *1938*, 2114.
285. Hasselstrom and Bogert, *J. Am. Chem. Soc.*, *57*, 1579 (1935).
286. Heiduschka, *Arch. Pharm.*, *244*, 569 (1906); *Centr.*, *1907*, I, 572.
287. Henriques, *Ber.*, *27*, 2993 (1894).
288. Hershberg and Fieser, *J. Am. Chem. Soc.*, *63*, 2561 (1941).
289. Herzfelder, *J. Chem. Soc.*, *67*, 640 (1895).
290. Herzog and Jolles, *Ber.*, *48*, 1574 (1915).
291. Herzog, *Ber.*, *51*, 516 (1918).
292. Herzog and Kreidl, *Ber.*, *B55*, 3394 (1922).
293. Hinsberg, *Ber.*, *43*, 901 (1910).
294. Hinsberg, *Ber.*, *56*, 2008 (1923).
295. Hixon and Cauwenberg, *J. Am. Chem. Soc.*, *52*, 2118, 2125 (1930).
296. Hjelt, *Ber.*, *22*, 2904 (1889).
297. Hollins, *Chem. Age (London)*, *11*, 416 (1924); *Chem. Abstracts*, *19*, 733 (1925).
298. Holzle, *Experientia*, *3*, 149 (1947); *Chem. Abstracts*, *42*, 2599 (1948).
299. Hooley, *Chem. Age* (*London*), *20*, No. 515, *Dyestuffs Monthly Suppl.*, 37–38 (1929); *Centr.*, *1929*, II, 1076.
300. Horton, *J. Org. Chem.*, *14*, 760 (1949).
301. Huntress and Hearon, *J. Am. Chem. Soc.*, *63*, 2762 (1941).
302. Huntress and Olsen, *J. Am. Chem. Soc.*, *70*, 2856 (1948).
303. Hurd and Greengard, *J. Am. Chem. Soc.*, *52*, 3356 (1930).
304. Hutchison and Smiles, *J. Chem. Soc.*, *101*, 570 (1912).
305. Jacoby, *Iowa State Coll. J. Sci.*, *13*, 70 (1938); *Chem. Abstracts*, *34*, 99 (1940).
306. Jain, Iyer, and Guha, *Science and Culture*, *11*, 270 (1945); *Chem. Abstracts*, *40*, 2125 (1946); *43*, 2597 (1949).
307. Jezierski, *Roczniki Chem.*, *14*, 216 (1934); *Chem. Abstracts*, *29*, 2161 (1935).
308. Jusa and Steckler, *Monatsh.*, *72*, 143 (1938).
309. Kadiera, *Ber.*, *38*, 3576 (1905); Ger. Pat., 106,511 (1899).
310. Kägi, *Helv. Chim. Acta*, *24*, 141E (1941).
311. Kalb and Bayer, *Ber.*, *46*, 3879 (1913).
312. Kalb and Berrer, *Ber.*, *B57*, 2105 (1924).
313. Kambli, *Helv. Chim. Acta*, *24*, 93E (1941).
314. Katz and Selman, *Z. Physik.*, *66*, 834 (1930); *Centr.*, *1931*, I, 2309.
315. Kiprianov and Timoshenko, *J. Gen. Chem.* (*U.S.S.R.*), *17*, 1468 (1947); *Chem. Abstracts*, *42*, 8477 (1948).
316. Kirjakka, *Soumen Kemistilehti*, *B13*, 22 (1940); *Chem. Abstracts*, *35*, 2508 (1941).
317. Kitamura, *J. Pharm. Soc. Japan*, *58*, 29 (1938); *Chem. Abstracts*, *32*, 3759 (1938)
318. Kitchen and Sandin, *J. Am. Chem. Soc.*, *67*, 1645 (1945).
319. Klatt, *Z. anorg. allg. Chem.*, *232*, 393 (1937); *Centr.*, II, 757 (1937).
320. Kneckt and Hibbert, *Ber.*, *40*, 3819 (1907).
321. Knott, *J. Chem. Soc.*, *1945*, 455.
322. Koenigs and Geisler, *Ber.*, *B57*, 2076 (1924).
323. Koenigs and Kantrowitz, *Ber.*, *B60*, 2097 (1927).
324. König and Hamprecht, *Ber.*, *B63*, 1546 (1930).
325. Kohlrausch and Seka, *Ber.*, *B71*, 1563 (1938).
325a. Komppa, *Ber.*, *26*, 277 (1893).
326. Komppa, *Ber.*, *26*, 2968 (1893).
327. Komppa, *Acta soc. sci. fennicae*, *23*, 1 (1897); *Centr.*, *1897*, II, 270.
328. Komppa, *J. prakt. Chem.*, *122*, 319 (1929); *Chem. Abstracts*, *24*, 112 (1930).
329. Komppa and Weckman, *J. prakt. Chem.* *138*, 109 (1933); *Chem. Abstracts*, *27*, 5326 (1933).

330. Komppa and Nyman, *J. prakt. Chem.*, *139*, 229 (1934); *Chem. Abstracts*, *28*, 2710 (1934).
331. Komppa, *Kgl. Norske Videnskab. Selskabs, Forh.*, *9*, 157 (1936); *Chem. Abstracts*, *31*, 7423 (1937).
332. Kramer and Weissgerber, *Ber.*, *34*, 1665 (1901).
333. Krollpfeiffer, Schultze, Schlumböhm, and Sommermeyer, *Ber.*, *B58*, 1654 (1925).
334. Krollpfeiffer, Branscheid, Thorn, and Schneider, *Ann.*, *462*, 46 (1928).
335. Krollpfeiffer and Schneider, *Ber.*, *B61*, 1284 (1928).
336. Kruber, *Ber.*, *B53*, 1566 (1920).
337. Kruber and Rappen, *Ber.*, *B73*, 1184 (1940).
338. Kunz and Günther, *Ber.*, *B56*, 2027 (1923).
339. Lambert and Lecomte, *Compt. rend.*, *208*, 1148 (1939).
340. Lanfry, *Compt. rend.*, *152*, 92 (1911).
341. Lanfry, *Compt. rend.*, *152*, 1254 (1911).
342. Lanfry, *Compt. rend.*, *154*, 519 (1912).
343. Lanfry, *Compt. rend.*, *155*, 1517 (1912).
344. Langer, *Ber.*, *17*, 1569 (1884).
345. Lefevre, *Rev. gén. mat. color.*, *11*, 257 (1907); *Chem. Abstracts*, *2*, 324 (1908).
346. Lesser and Weiss, *Ber.*, *45*, 1835 (1912).
347. Lesser and Weiss, *Ber.*, *46*, 2640 (1913).
348. Lesser and Schoeller, *Ber.*, *47*, 2292 (1914).
349. Levkoev, Sveshnikov, and Durmashkina, *J. Gen. Chem.* (*U.S.S.R.*), *10*, 773 (1940); *Chem. Abstracts*, *35*, 2327 (1941).
350. Ley and Specker, *Z. wiss. Phot.*, *38*, 12 (1939); *Chem. Abstracts*, *34*, 4992 (1940).
351. Liebermann and Zsuffa, *Ber.*, *44*, 854 (1911).
352. Lifschitz and Lourie, *Ber.*, *50*, 897 (1917).
353. Linstead, Noble, and Wright, *J. Chem. Soc.*, *1937*, 911.
354. Luck, *Färberztg.*, *18*, 33 (1907); *Chem. Abstracts*, *1*, 1063 (1907).
355. Lulek, *Ind. Eng. Chem.*, *23*, 96 (1931).
356. Lustig and Paulus, *Bull. soc. ind. Mulhouse*, *95*, 752 (1929); Wagner, *ibid.*, 753; *Chem. Abstracts*, *24*, 2298 (1930).
357. Lüttringhaus, Wagner-von Sääf, Sucher, and Borth, *Ann.*, *557*, 25 (1945).
358. McClelland, *J. Chem. Soc.*, *1929*, 1588.
359. McClelland and D'Silva, *J. Chem. Soc.*, *1931*, 2972.
360. McClelland and D'Silva, *J. Chem. Soc.*, *1932*, 227.
361. McClelland, Rose, and Bartlett, *J. Chem. Soc.*, *1940*, 323.
362. McClelland and Smith, *J. Chem. Soc.*, *1945*, 408.
363. McClelland and Stammers, *J. Chem. Soc.*, *1948*, 78.
364. McClelland, Rose, and Stammers, *J. Chem. Soc.*, *1948*, 81.
365. MacBeth and Craik, *Proc. Roy. Irish Acad.*, *B37*, 53 (1925); *Chem. Abstracts*, *19*, 2951 (1925).
366. Machemer, *J. prakt. Chem.*, *127*, 109 (1930); *Chem. Abstracts*, *25*, 103 (1931).
367. Maihle, *J. usines gaz*, *45*, 209 (1921); *Chem. Abstracts*, *15*, 3201 (1921).
368. Mann and Haworth, *J. Chem. Soc.*, *1944*, 670.
369. Mazoni-Ansidei, *Ricerca sci.*, *8*, II, No. 3–4, 2 pp. (1937); *Chem. Abstracts*, *32*, 4879 (1938).
370. Marschalk, *Ber.*, *45*, 1481 (1912).
371. Marschalk, *J. prakt. Chem.*, *88*, 227 (1913).
372. Marschalk, *J. prakt. Chem.*, *88*, 246 (1913).
373. Marschalk, *Bull. soc. chim. France*, *9*, 801 (1942).
374. Martin, *Z. fur Farbenind.*, *5*, 185 (1906); *Centr.*, *1906*, II, 286.
375. Maruyama, *Bull. Inst. Phys. Chem. Research* (*Tokyo*), *18*, 1165 (1939); *Chem. Abstracts*, *34*, 6817 (1940).
376. Maxted and Walker, *J. Chem. Soc.*, *1948*, 1916.
377. Maxted, *J. Soc. Chem. Ind.*, *67*, 93 (1948).

378. Mayer *et al.*, *Ann.*, *488*, 259 (1931).
379. Mazza and Solazzo, *Rend. accad. sci. Napoli*, *33* (3), 236 (1927); *Chem. Abstracts*, *23*, 2417 (1929).
380. Mazza and Melchionna, *Rend. accad. sci. Napoli*, *34* (3), 54 (1928); *Chem. Abstracts*, *23*, 2956 (1929).
381. Mentzer, Billet, Mohlo, and Dat Xuong, *Bull. soc. chim. France*, *12*, 161 (1945).
382. Mentzer and Billet, *Bull. soc. chim. France*, *12*, 292 (1945).
383. A. Meyer, *Compt. rend.*, *156*, 714 (1913).
384. R. Meyer, *Ber.*, *33*, 2570 (1900).
385. R. Meyer and Wesche, *Ber.*, *50*, 422 (1917).
386. R. Meyer and W. Meyer, *Ber.*, *51*, 1571 (1918).
387. R. Meyer and W. Meyer, *Ber.*, *B52*, 1249 (1919).
388. V. Meyer, *Ber.*, *19*, 1432 (1886).
389. Minaev and Nikolaeva, *Anilinokrasochnaya Prom.*, *3*, 258 (1933); *Chem. Abstracts*, *28*, 899 (1934).
390. Mitra, *J. Indian Chem. Soc.*, *15*, 62 (1938); *Chem. Abstracts*, *32*, 4983(1938).
391. Moore and Greensfelder, *J. Am. Chem. Soc.*, *69*, 2008 (1947).
392. Muth and Putzer, PBL 63,936, Fiat Microfilm Reel C60, PB 17,657
393. Nakanishi, *Sci. Papers Inst. Phys. Chem. Res.*, *13*, Nr. 246–253 (1930); *Centr.*, *1930*, II, 2831.
394. Naumow and JePissarewa, *Cotton Ind.* (*U.S.S.R.*), *10*, 41 (1940); *Centr.*, *1941*, II, 2497.
395. Neumoyer and Amschutz, *J. Am. Chem. Soc.*, *66*, 1680 (1944).
396. Neumoyer and Amschutz, *J. Am. Chem. Soc.*, *69*, 1920 (1947).
397. Noelting, *Ann. chim.*, *19* (8), 534 (1910).
398. Noelting and Steuer, *Ber.*, *43*, 3512 (1910).
399. Noelting and Herzbaum, *Ber.*, *44*, 2585 (1911).
400. O'Brochtu and Lowy, *J. Am. Chem. Soc.*, *61*, 2765 (1939).
401. Ogata, *J. Chem. Soc. Japan*, *55*, 394 (1934); *Chem. Abstracts*, *28*, 5817 (1934).
402. Orlov and Samovskaya, *Anilinokrasochnaya Prom.* *4*, 144 (1934); *Chem. Abstracts*, *28*, 5673 (1934).
403. Papa, Schwenk, and Ginsberg, *J. Org. Chem.*, *14*, 723 (1949).
404. Pearson, *Z. ges. textilind.*, *38*, 311 (1935); *Centr.*, *1935*, II, 1615.
405. Peters, *J. Chem. Soc.*, *1942*, 562.
406. Peters, *J. Chem. Soc.*, *1947*, 742.
407. Plazek and Sucharda, *Roczniki Chem.*, *7*, 187 (1927); *Centr.*, *1928*, I, 2091.
408. Plazek and Sucharda, *Ber.*, *B59*, 2282 (1926).
409. Pollak, Krauss, and Lustig, *Monatsh.*, *55*, 358 (1930).
410. Posner and Wallis, *Ber.*, *B57*, 1673 (1924).
411. Posner, Zimmermann, and Kautz, *Ber.*, *B62*, 2150 (1929).
412. Preisler and Hempelmann, *J. Am. Chem. Soc.*, *58*, 2305 (1936).
413. Prelog and Cerkovnikov, *Ann.*, *537*, 214 (1939).
414. Prescott and Smiles, *Proc. Chem. Soc.*, *27*, 317 (1913); *Chem. Abstracts*, *7*, 2926 (1913).
415. Price and Smiles, *J. Chem. Soc.*, *1928*, 2858.
416. Pummerer, *Ber.*, *42*, 2275 (1909).
417. Pummerer, *Ber.*, *43*, 1370 (1910).
418. Pummerer, *Ber.* *44*, 338 (1911).
419. Pummerer, *Ber.*, *44*, 346 (1911).
420. Pummerer and Luther, *Ber.*, *B64*, 831(1931).
421. Ralston and Christensen, *Ind. Eng. Chem.*, *29*, 194 (1937).
422. Remick, *J. Am. Chem. Soc.*, *58*, 733 (1936).
423. Riesz and Hübsch, *Monatsh.*, *53*, *54*, 111 (1929).
424. Riesz, Pollak, and Wittels, *Ann.*, *487*, 264 (1931).
425. Riesz, *Ber.*, *B64*, 1893 (1931).

426. Rodionov and Bogoslovskii, *J. Gen. Chem. (U.S.S.R.)*, *7*, 2685 (1937); *Chem. Abstracts*, *32*, 2939 (1938).
427. Rodionov, Bogoslovskii, and Kazakova, *J. Gen. Chem. (U.S.S.R.)*, *18*, 1898 (1948); *Chem. Abstracts*, *43*, 3816 (1949).
428. Rodionov, Bogoslovskii, and Kazakova, *J. Applied Chem. (U.S.S.R.)*, *21*, 962 (1948); *Chem. Abstracts*, *43*, 6204 (1949).
429. deRoy and van Zuydewijn, *Rec. trav. chim.*, *57*, 445 (1938).
430. Rosenberg, *Farber.-Ztg.*, *19*, 101, 119 (1908); *Z. angew. Chem.*, *21*, 961, (1909); *Chem. Abstracts*, *3*, 489 (1909).
431. Rosenberg, *Z. angew. Chem.*, *22*, 2129 (1909); *Chem. Abstracts*, *4*, 672 (1910).
432. Ruggli and Disler, *Helv. Chim. Acta*, *10*, 938 (1927).
433. Ruggli and Heitz, *Helv. Chim. Acta*, *14*, 257 (1931).
434. Rumpf, *Bull. soc. chim. France*, *9*, 661 (1942).
435. Raeman, *Dyer Calico Printer*, *64*, 87 (1930); *Centr.*, *1930*, II, 2190.
436. Sachs and Oeholm, *Ber.*, *47*, 955 (1914).
437. Sander, *Ber.*, *58*, 824 (1925).
438. Sandin and Fieser, *J. Am. Chem. Soc.*, *62*, 3098 (1940).
439. Sandin and Kitchen, *J. Am. Chem. Soc.*, *67*, 1305 (1945).
440. Sawlewicz, *Roczniki Chem.*, *16*, 470 (1936); *Chem. Abstracts*, *31*, 2186 (1937).
441. Schoeller, *Ueber Seleno-Naphthen-chinon, Oldenburg;* G. Stallings Verlag, 1915; *Chem. Abstracts*, *9*, 1919 (1915).
442. Scholl and Seer, *Ann.*, *394*, 111 (1912).
443. Schönberg, *Ber.*, *B56*, 2275 (1923).
444. Schönberg and Vargha, *Ber.*, *B64*, 1390 (1931).
445. Schonberg, Petersen, and Kaltschmitt, *Ber.*, *B66*, 233 (1933).
446. Schönberg, Moubasher, and Mostafa, *J. Chem. Soc.*, *1941*, 348.
447. Schonberg and Mustafa, *J. Chem. Soc.*, *1945*, 657.
448. Schönberg and Asker, *J. Chem. Soc.*, *1946*, 604.
449. Schönberg and Asker, *J. Chem. Soc.*, *1946*, 609.
450. Schwecten, *Ber.*, *B65*, 1608 (1932).
451. Schwenk, *Biochem. Z.*, *72*, 383 (1916); *Chem. Abstracts*, *10*, 939 (1916).
452. Schwenk, *J. prakt. Chem.*, *103*, 103 (1921); *Chem. Abstracts*, *16*, 1078 (1922).
453. Sheppard, Newsome, and Brigham, *J. Am. Chem. Soc.*, *64*, 2923 (1942).
454. Sibata and Nishi, *J. Soc. Chem. Ind. Japan*, *39*, Suppl. Bind., 280 (1936); *Chem. Abstracts*, *30*, 8623 (1936).
455. Sibata and Okuyama, *J. Soc. Chem. Ind. Japan*, *39*, Suppl. Bind., 282 (1936); *Chem. Abstracts*, *30*, 8624 (1936).
456. Sibata and Sassa, *J. Soc. Chem. Ind. Japan*, *39*, Suppl. Bind., 283 (1936); *Chem. Abstracts*, *25*, 8624 (1936).
457. Sibata and Umezima, *J. Soc. Chem. Ind. Japan*, *42*, Suppl. Bind., 37 (1939); *Chem. Abstracts*, *33*, 6305 (1939).
458. Sibata, Sasa, and Umezima, *J. Soc. Chem. Ind. Japan*, *42*, Suppl. Bind. 38 (1939); *Chem. Abstracts*, *33*, 6305 (1939).
459. Shriner, Struck, and Jorison, *J. Am. Chem. Soc.*, *52*, 2060 (1930).
460. Smiles and Ghosh, *J. Chem. Soc.*, *107*, 1377 (1915).
461. Smiles and McClelland, *J. Chem. Soc.*, *119*, 1810 (1921).
462. Smiles and Hart, *J. Chem. Soc.*, *123*, 2907 (1923).
463. Smith and Melvin, *J. Econ. Entomol.*, *36*, 475 (1943); *Chem. Abstracts*, *38*, 208 (1944).
464. Staudinger and Siegwart, *Helv. Chim. Acta*, *3*, 840 (1920).
465. Steinkopf and Lützendorff, *Chem. Ztg.*, *36*, 379 (1913); *Chem. Abstracts*, *7*, 1482 (1913).
466. Steinkopf and Lützendorff, *Ann.*, *403*, 45 (1914).
467. Steinkopf and Butkiewicz, *Ann.*, *407*, 94 (1914).
468. Steinkopf and Augestad-Jensen, *Ann.*, *428*, 157 (1922).

469. Steinkopf, Beilenberg, and Augestad-Jensen, *Ann.*, *430*, 63 (1923)
470. Steinkopf and Wolfram, *Ann.*, *437*, 22 (1924).
471. Steinkopf and Höpner, *Ann.*, *501*, 174 (1933).
472. Steinkopf, Jacob, and Penz, *Ann.*, *512*, 136 (1934).
473. Steinkopf, *Ann.*, *513*, 281 (1934).
474. Steinkopf, *Ann.*, *519*, 297 (1935).
475. Steinkopf and Kohler, *Ann.*, *522*, 17 (1936).
476. Steinkopf and Gunther, *Ann.*, *522*, 28 (1936).
477. Steinkopf, Rosler, and Setzer, *Ann.*, *522*, 35 (1936).
478. Steinkopf, Schmitt, and Fiedler, *Ann.*, *527*, 237 (1937).
479. Steinkopf, *Ann.*, *532*, 282 (1937).
480. Steinkopf and Schmitt, *Ann.*, *533*, 264 (1938).
481. Steinkopf and Eger, *Ann.*, *533*, 270 (1938).
482. Steinkopf, Poulsson, and Herdey, *Ann.*, *536*, 128 (1938).
483. Steinkopf and Thormann, *Ann.*, *540*, 1 (1939).
484. Steinkopf, Barlag, and von Petersdorff, *Ann.*, *540*, 7 (1939).
485. Steinkopf, Leitsmann, Müller, and Wilhelm, *Ann.*, *541*, 260 (1939).
486. Steinkopf and Kühnel, *Ann.*, *545*, 33 (1940).
487. Steinkopf and Nitschke, *Arch. Pharm.*, *278*, 360 (1940); *Chem. Abstracts*, *35*, 3629 (1941).
488. Steinkopf and Engelmann, *Ann.*, *546*, 205 (1941).
489. Stenhouse, *Ann.*, *156*, 332 (1870).
490. Stollé, *Ber.*, *47*, 1130 (1914).
491. Stollé and Knebel, *Ber.*, *54*, 1213 (1921).
492. Stollé, Geisel, and Badstübner, *Ber.*, *58*, 2095 (1925).
493. Stollé and Badstübner, *J. prakt. Chem.*, (2), *121*, 266 (1929); *Chem. Abstracts*, *23*, 3470 (1929).
494. Stollé *et al.*, *J. prakt. Chem.*, (2), *128*, 1 (1930); *Chem. Abstracts*, *25*, 293 (1931).
495. Stollé and Badstübner, *J. prakt. Chem.*, *129*, 309 (1931); *Chem. Abstracts*, *25*, 2721 (1931).
496. Surrey, Hammer, and Suter, *J. Am. Chem Soc.*, *66*, 1933 (1944).
497. Sveshnikov and Levkoev, *J. Gen. Chem.* (*U.S.S.R.*), *10*, 274 (1940); *Chem. Abstracts*, *34*, 7111 (1940).
498. Sveshnikov, Levkoev, and Durmashkina, *J. Gen. Chem.* (*U.S.S.R.*), *14*, 198 (1944).
499. Szperl, *Roczniki Chem.*, *10*, 652 (1930); *Chem. Abstracts*, *25*, 938 (1931).
500. Szperl and Morawski, *Roczniki Chem.*, *10*, 657 (1930); *Chem. Abstracts*, *25*, 938 (1931).
501. Szperl and Böhm, *Roczniki Chem.*, *12*, 378 (1932); *Chem. Abstracts*, *27*, 3926 (1933).
502. Szperl and Chmielnicka, *Roczniki Chem.*, *16*, 101 (1936); *Chem. Abstracts*, *31*, 2186 (1937).
503. Szperl, *Roczniki Chem.*, *18*, 804 (1938); *Chem. Abstracts*, *33*, 6304 (1939).
504. Tarbell, Fukushima, and Dam, *J. Am. Chem. Soc.*, *67*, 1643 (1945).
505. Tarbell and Fukushima, *J. Am. Chem. Soc.*, *68*, 1456 (1946).
506. Täuber, *Chem. Ztg.*, *32*, 1032 (1908); *Chem. Abstracts*, *3*, 596 (1909).
507. Täuber, *Chem. Ztg.*, *33*, 341 (1909); *Chem. Abstracts*, *3*, 2062 (1909).
508. Thomas, De Eds, and Cox, *Food Research*, *7*, 161 (1942); *Chem. Abstracts*, *36*, 4194 (1942).
509. Tolber, *Ber.*, *B66*, 1757 (1933).
510. Treadwell, Dreyfuss, and Bossi, *Helv. Chim. Acta*, *5*, 732 (1922).
511. Umezawa, *Bull. Chem. Soc. Japan*, *14*, 363 (1939); *Chem. Abstracts*, *34*, 1309 (1940).
512. Vernet, *Arch. sci. phys. nat.*, *35*, 148 (1931); *Chem. Abstracts*, *25*, 1976 (1931).
513. Vozhdaeva, *J. Applied Chem.* (*U.S.S.R.*), *13*, 1620 (1940); *Chem. Abstracts*, *35*, 3819 (1941).

514. von Wacek, Eppinger, and von Bézard, *Ber.*, *B73*, 521 (1940).
515. Wahl and Bagard, *Bull. soc. chim. France*, (4) *15*, 336 (1914).
516. Watson and Dutt, *J. Chem. Soc.*, *121*, 2418 (1922).
517. Weber, *Am. Dyestuff Reporter*, *22*, 157 (1933); *Centr.*, *1933*, I, 2747.
518. Wegler and Binder, *Arch. Pharm.*, *275*, 506 (1937); *Chem. Abstracts*, *32*, 939 (1938).
519. Wegmann and Dahn, *Helv. Chim. Acta*, *29*, 415 (1946).
520. Wegscheider and Joachimowitz, *Montash.*, *35*, 1046 (1914).
521. Weinberg, *Ber.*, *A63*, 117 (1930).
522. Weissgerber and Kruber, *Ber.*, *B53*, 1551 (1920).
523. Weissgerber, *Brennstoff Chem.*, *2*, 1 (1921); *Chem. Abstracts*, *15*, 941 (1921).
524. Weissgerber and Seidler, *Ber.*, *60*, 2088 (1927).
525. Werner, *Rec. trav. chim.*, *68*, 509 (1949).
526. Werner, *Rec. trav. chim.*, *68*, 520 (1949).
527. Weston and Suter, *J. Am. Chem. Soc.*, *61*, 389 (1938).
528. Winter, *Deut. Farber-Ztg.*, *43*, 826 (1907); *Chem. Abstracts*, *2*, 710 (1908).
529. Wirther, *Farber-Ztg.*, *18*, 161 (1906); *Chem. Abstracts*, *1*, 2493 (1907).
530. Wray, *Text. Color*, *335*, 321 (1906); *Chem. Abstracts*, *1*, 640 (1907).
531. Reitzenstein, *J. prakt. Chem.*, (2), *82*, 262 (1910); *Beils*, Suppl. Vol. XVII–XIX, pp. 590, 602.
532. Reitzenstein and Fitzgerald, *J. prakt. Chem.*, (2), *89*, 278 (1914); *Beils*, Suppl. Vol. XVII–XIX, p. 590, 602.
533. King and Nord, *J. Org. Chem.*, *13*, 635 (1948).
534. Longuet-Higgins, *Acta Crystallog.*, *3*, 76 (1950).
535. Cagniant, *Compt. rend.*, *230*, 100 (1950).
536. Buu-Hoï, *J. Chem. Soc.*, *1949*, 2882.
537. Szmuszkovicz and Modest, *J. Am. Chem. Soc.*, *72*, 571 (1950).
538. Modest and Szmuszkovicz, *J. Am. Chem. Soc.*, *72*, 577 (1950).
539. Barieau and Barusch, Preprints of Symposium on Organic Sulfur Compounds of the Division of Petroleum Chemistry, *1949*, 197.
540. Bordwell *et al.*, *ibid.*, pp. 75–81.
541. Leser, *Ber.*, *17*, 1824 (1884).
542. Autenreith and Brüning, *Ber.*, *36*, 183 (1903).
543. Miller and Nord, *J. Org. Chem.*, *15*, 89 (1950).
544. Farrar and Levine, *J. Am. Chem. Soc.*, *72*, 4433 (1950).
545. Cagniant, *Compt. rend.*, *229*, 1342 (1949).
546. Weston and Michaels, *J. Am. Chem. Soc.*, *72*, 1422 (1950).
547. Thianaphthene, Technical Bulletin of Jefferson Chemical Company, Inc.
548. Mozingo *et al.*, *J. Am. Chem. Soc.*, *67*, 2092 (1945).
549. Cheney and Piening, *J. Am. Chem. Soc.*, *67*, 729, 731 (1945).
550. Leandri, *Gazz. chim. ital.*, *79*, 286 (1949); *Chem. Abstracts*, *44*, 2984 (1950).
551. Diesbach and Heppner, *Helv. Chim. Acta*, *32*, 687 (1949); *Brit. Abstracts*, AII, *1950*, 53.
552. Biedermann and Jacobsen, *Ber.*, *19*, 2444 (1886).
553. Hanna and Smith, *Am. Chem. J.*, *21*, 381 (1899).
554. Capelle, *Bull. soc. chim. France*, (4) *3*, 150 (1908).
555. deConinck, *Bull. acad. roy. Belg., Class sci.*, *1908*, 303.
556. Briscoe and Peel, *J. Chem. Soc.*, *1928*, 1741.
557. Peel and Robinson, *J. Chem. Soc.*, *1928*, 2068.
558. Bhatt, Nargund, Kanga, and Shah, *J. Univ. Bombay*, *3*, 159 (1934); *Chem. Abstracts*, *29*, 4762 (1935).
559. Challenger and Harrison, *J. Inst. Petroleum Technol.*, *21*, 135 (1935).
560. Challenger and Gibson, *J. Chem. Soc.*, *1940*, 305.
561. Bruce, Challenger, Gibson, and Allenby, *J. Inst. Petroleum Technol.*, *34*, 226 (1948).

562. Challenger, Clapham, and Emmott, *J. Inst. Petroleum Technol.*, *34*, 922 (1948).
563. Steinkopf and Petersdorff, *Ann.*, *543*, 119 (1940).
564. Friedmann, *Ber.*, *49*, 1551 (1916).
565. Friedmann, *Ber.*, *49*, 1344 (1916).
566. Friedmann, *Refiner*, *20*, 395 (1941).
567. Nürsten and Peters, *J. Chem. Soc.*, *1950*, 729.
568. Farmer and Shipley, *J. Chem. Soc.*, *1947*, 1519.
569. Naylor, *J. Chem. Soc.*, *1947*, 1532.
570. Naylor, *J. Chem. Soc.*, *1949*, 2749.
571. Truttwin, *Enzyklapodie der Küpfenfarbstaffe*, Springer, Berlin, 1920. This reference contains a complete bibliography on thioindigo dyes up to 1920.
572. Voss, *Dissertation*, Darmstadt, 1916.
573. Krollpfeiffer, Hartmann, and Schmidt, *Ann.*, *563*, 15 (1949).
574. Krollpfeiffer, Schneider, and Wissner, *Ann.*, *566*, 139 (1950).
575. Fox, *Vat Dyestuffs*, Chapman and Hall, London, 1946.
576. Diserens, *Die neuesten Fortschritte in der Avwendung der Farbstoffe*, Virkhauser, Basel, 1946.
577. BIOS/DOCS/1156/983/22, I.G. Farbenindustrie, *Manufacture of Thioindigoid and Sulfur Dyestuffs at Hoechst and Mainkur*.
578. BIOS/DOCS/2351/1482/22, *Manufacture of Miscellaneous Dyestuffs*.
579. Verley, *Bull. soc. chim. France*, (3) *25*, 46 (1901).
580. Bury, *J. Am. Chem. Soc.*, *57*, 2115 (1935).
581. Witt, *Ber.*, *9*, 522 (1876); *Ber.*, *21*, 321 (1888).
582. Baeyer, *Ann.*, *354*, 152 (1907).
583. Martinet, *Rév. gen. mat. color*, *25*, 17 (1925).
584. Baeyer, *Ber.*, *12*, 1311 (1879)
585. V. Meyer, *Ber.*, *16*, 1477 (1883).
586. V. Meyer, *Ber.*, *16*, 2971 (1883).
587. Baeyer and Lazarus, *Ber.*, *18*, 2637 (1885).
588. Tohl, *Ber*, *27*, 667 (1894).
589. Friedländer and Weisberg, *Ber.*, *28*, 1641 (1895).
590. Leibermann and Pleus, *Ber.*, *37*, 2461 (1904).
591. Storch, *Ber.*, *37*, 1961 (1904).
592. Bauer, *Ber.*, *37*, 1244 (1904).
593. Oster, *Ber.*, *37*, 3348 (1904).
594. Bauer, *Ber.*, *37*, 3128 (1904).
595. Liebermann and Krauss, *Ber.*, *40*, 2499 (1907).
596. Wray, *J. Soc. Chem. Ind.*, *38*, 87T (1919).
597. Schlenk and Blum, *Ann.*, *433*, 95 (1923).
598. Heller, *Z. angew. Chem.*, *37*, 1017 (1924); *Chem. Abstracts*, *19*, 1277 (1925).
599. Steinkopf and Roch, *Ann.*, *482*, 251 (1930).
600. Steinkopf and Hemple, *Ann.*, *495*, 144 (1932).
601. Steinkopf and Hanske, *Ann.*, *541*, 238 (1939).
602. Steinkopf and Wilhelm, *Ann.*, *546*, 211 (1941).
603. Meisel, Johnson, and Hartough, *J. Am. Chem. Soc.*, *72*, 1910 (1950).
604. Gilman and Nobis, *J. Am. Chem. Soc.*, *72*, 2629 (1950).
605. Shirley and Cameron, *J. Am. Chem. Soc.*, *72*, 2788 (1950).
606. Renard, *Bull. soc. chim. France*, (3), *3*, 958 (1889).
607. Renard, *Bull. soc. chim. France*, (3), *5*, 278 (1891).
608. Herz, *J. Am. Chem. Soc.*, *72*, 4999 (1950).
609. Smith and Boyer, *J. Am. Chem. Soc.*, *73*, 2626 (1951).
610. Renard, *Compt. rend.*, III, 48 (1890).
611. Friedmann, *Ber.*, *49*, 277, 1344, 1352, 1551 (1916).
612. Herz, *J. Am. Chem. Soc.*, *73*, 351 (1951).
613. Buu-Hoï and Royer, *Rec. trav. chim.*, *69*, 861 (1950).

614. Schmidt and Seilert, *Ann.*, *562*, 15 (1949).
615. Buu-Hoï, Hoán, and Khôi, *J. Org. Chem.*, *15*, 957 (1950).
616. Hoffmann *et al.*, *J. Biol. Chem.*, *145*, 503 (1942).
617. Blicke, in Elderfeld, ed., *Heterocyclic Compounds*, Chapter V, Wiley, New York, 1950.
618. Dewar, *J. Chem. Soc.*, *1950*, 2329.
619. Pausacker and Schubert, *J. Chem. Soc.*, *1950*, 1814.
620. Koelsch and Stephens, *J. Am. Chem. Soc.*, *72*, 2209 (1950).
621. King and Nord, *J. Org. Chem.*, *13*, 635 (1948).
622. Hartough *et al.*, *J. Am. Chem. Soc.*, *68*, 2639 (1946); *69*, 1012, 1014, 3093 (1947): *70*, 867 (1948). Heid and Levine, *J. Org. Chem.*, *13*, 409 (1948). Given and Hammick, *J. Chem. Soc.*, *1947*, 1237.
623. Hartough, *J. Chem. Ed.*, *27*, 500 (1950).
624. Buu-Hoï, Hoán, and Khôi, *Rec. trav. chim.*, *69*, 1053 (1950).
625. Buu-Hoï, Hoán, and Xuong, *Rec. trav. chim.*, *69*, 1083 (1950).
626. Hoog, *Rec. trav. chim.*, *69*, 1289 (1950).
627. Kao, Tilak, and Venkataraman, *Proc. Indian Acad. Sci.*, *A32*, 162 (1950).
628. Bordwell, private communication to the authors.
629. Buehler, Harris, and Arendale, *J. Am. Chem. Soc.*, *72*, 4953 (1950).
630. Simonis and Remmert, *Ber.*, *48*, 208 (1915).
631. Tamamusi, Akiyama, and Umezawa, *Chem. Abstracts*, *34*, 424 (1940); *Bull. Chem. Soc. Japan*, *14*, 318 (1939).
632. Umezawa, *Chem. Abstracts*, *34*, 1309 (1940); *ibid.*, *14*, 363 (1939).
633. Wyman and Brode, Abstract of Papers, 118th Meeting of the ACS, Chicago, Sept. 1949.
634. Selch, *Monats. Chem.*, *14*, 3 (1893), *Ber.*, Ref. *26*, 233 (1893).
635. Miller, Miller, Sandin, and Brown, *Cancer Research*, *9*, 504 (1949).
636. Buu-Hoï and Royer, *Rec. trav. chim.*, *69*, 861 (1950).
637. Cagniant, *Compt. rend.*, *226*, 1376 (1948).
638. Cross and Snyder, *Soap Sanit. Chemicals*, *25*, No. 2, 135 (1949).
639. Merkel and Wiegand, *Z. Naturforsch.*, *3b*, 93 (1948).
640, Henecka, *Chem. Ber.*, *81*, 179 (1948).
641. Hughes, *Bull. Johns Hopkins Hospital*, *82*, 338 (1948).
642. Feiser *et al.*, *J. Am. Chem. Soc.*, *70*, 3212 (1948).
643. Rodionov, Bogoslovskiĭ, and Kazakova, *Izvest. Akad. Nauk S.S.S.R.*, *Otdel Khim. Nauk*, *1948*, 536; *Chem. Abstracts*, *43*, 2200 (1949).
644. Schulze and Becker, *Holzforschung*, *2*, 97 (1948); *Chem. Abstracts*, *43*, 4417 (1949).
645. Reissert and Holle, *Ber.*, *44*, 3029 (1911).
646. Mowry, Ringwald, and Renoll, *J. Am. Chem. Soc.*, *71*, 120 (1949).
647. Paal, *Ber.*, *18*, 2251 (1885).
648. Gilman and Jacoby, private communication.
649. Gilman and Lentz, private communication.
650. Gilman and Ingham, private communication.
650a. Gilman and Webb, *J. Am. Chem. Soc.*, *71*, 4062 (1949).
651. Gilman and Esmay, private communication.
652. Hartough, *Anal. Chem.*, *23*, 1128 (1951).
653. McCullough, Campbell, and Gould, *J. Am. Chem. Soc.*, *72*, 5753 (1950).
654. Block, *J. Am. Chem. Soc.*, *72*, 5641 (1950).
655. Cullinune, *J. Chem. Soc.*, *1930*, 2267.
656. Bass, *Thesis*, Yale University, 1929.
657. Gilman, Illumitate, and Nobis, private communication.
658. Gilman and Van Ess, *J. Am. Chem. Soc.*, *55*, 1258 (1933).
659. Gilman, Van Ess, and Hayes, *ibid.*, *61*, 643 (1939).
660. Gilman, Esmay, and Ingham, *J. Am. Chem. Soc.*, *73*, 470 (1951).

661. Brown *et al.*, *J. Am. Chem. Soc.*, *73*, 465 (1951).
662. Gilman, private communication.
663. Gilman and Marshal, *J. Am. Chem. Soc.*, *71*, 2066 (1949).
664. Tominaga, Hazato, and Oshina, *J. Chem. Soc. Japan*, *64*, 1291 (1943); *Chem. Abstracts*, *41*, 3334 (1947).
665. Armstrong *et al.*, *J. Chem. Soc.*, *1950*, 3359.
666. Moubasher *et al.*, *J. Chem. Soc.*, *1950*, 1998.
667. Friedman, *Ber.*, *49*, 1352 (1916).
668. Brown and Goncalves, Abstracts of 117th Meeting of American Chemical Society, Philadelphia.
669. Buu-Hoï, Hoán, Khôi, and Xuong, *J. Org. Chem.*, *16*, 309 (1951).
670. Meyer, *Monatsh.*, *36*, 723 (1915).
671. Mascarelli *et al.*, *Gazz. chem. ital*, *59*, 867 (1929).
672. Rule and Brown, *J. Chem. Soc.*, 175 (1932).
673. Gilman and Ingham, *J. Am. Chem. Soc.*, *73*, 4982 (1951).
674. Hurd and Kreuz, *J. Am. Chem. Soc.*, *72*, 5546 (1950).
675. Burtner and Brown, *J. Am. Chem. Soc.*, *73*, 879 (1951).
676. Buu-Hoï and Hoán, *J. Chem. Soc.*, *1951*, 251.
677. Bordwell and McKellin, *J. Am. Chem. Soc.*, *73*, 2251 (1951).
678. Brown and Goncalves, private communication.
679. Dann, private communication.
680. Hammett, *Physical Organic Chemistry*, McGraw-Hill, New York, 1940, p. 188.
681. Pauling, *The Nature of the Chemical Bond*, Cornell Univ. Press, Ithaca, N.Y., 1944, p. 60.
682. Alexander, *Ionic Organic Reactions*, Wiley, New York, 1950, p. 16.
683. Shah, Tilak, and Venkataiman, *Proc. Indian Acad. Sci.*, *A28*, 142–150; *Chem. Abstracts*, *44*, 3938 (1950).
684. Peck and Folkers, in *Chemistry of Penicillin*, H. T. Clarke *et al.* eds., Princeton Univ. Press, 1944, pp. 52–75; *Chem. Abstracts*, *44*, 9416 (1950).
685. Eagle and Anton, *J. Pharmacol. Exptl. Therap.*, *99*, No. 4, Pt. 1, 450–7 (1950); *Chem. Abstracts*, *44*, 10, 156 (1950).
686. Remick, *Electronic Interpretations of Organic Chemistry*, 2nd ed., Chapter V, Wiley, New York, 1949.
686a. Remick, *Electronic Interpretations of Organic Chemistry*, 2nd ed., Wiley, New York, 1949, p. 372.
687. Gilman, Calloway, and Burtner, *J. Am. Chem. Soc.*, *57*, 906 (1935).
688. Schomaker and Pauling, *J. Am. Chem. Soc.*, *61*, 1779 (1939).
689. Dewar, *Electronic Theory of Organic Chemistry*, Clarendon Press, Oxford, 1949, p. 189.
690. Henne and Kaye, *J. Am. Chem. Soc.*, *72*, 3369 (1950).
691. Suginome and Umezawa, *Bull. Chem. Soc. Japan*, *11*, 157 (1936); *Chem. Abstracts*, *30*, 5981 (1936).
692. Gilman and Burtner, *J. Am. Chem. Soc.*, *55*, 2903 (1933).
693. Stoermer and Kahlert, *Ber.*, *35*. 1640 (1902).
694. Stoermer and Richter, *Ber.*, *30*, 2094 (1897).
695. Waters, *Physical Aspects of Organic Chemistry*, Van Nostrand, New York, 1950, p. 497.
696. Waters, *loc. cit.*, p. 502.
697. Roberts and Curtin, *J. Am. Chem. Soc.*, *68*, 1658 (1946).
698. Fieser and Fieser, *Organic Chemistry*, 2nd ed., Reinhold, New York, 1950, p. 754.
699. Appleby *et al.*, *J. Am. Chem. Soc.*, *70*, 1552 (1948).
700. Hartough, *Thiophene and Its Derivatives*, Interscience, New York, 1952.
701. Backer and Melles, *Proc. Koninkl. Nederland-Akad. Wetenschap.*, *54*, 340 (1951).
702. Dutta and Chaudhury, *J. Ind. Chem. Soc.*, *28*, 169 (1951).
703. Chaudhury and Dutta, *J. Ind. Chem. Soc.*, *28*, 175 (1951).

704. Backer and Kloosterziel, *Proc. Koninkl. Ned. Akad. Wetenschap.*, *53*, 1507 (1950); *Chem. Abstracts*, *45*, 9028 (1951).
705. Cagniant, *Compt. rend.*, *232*, 734 (1951).
706. Trinh, *Compt. rend.*, *232*, 2023 (1951).
707. Levkoev, Sveshnikov, and Lifshits, *Doklady Akad. Nauk S.S.S.R.*, *74*, 275 (1950); *Chem. Abstracts*, *45*, 9526 (1951).
708. Rodoinov, Bogoslovskii, and Kazakova, *Zhur. Priklad. Khim.* (*J. Applied Chem.*), *24*, 670 (1951); *Chem. Abstracts*, *46*, 741 (1952).
709. Gillet, *Bull. soc. chim. France*, *1950*, 1141.
710. Jenny, *Helv. Chim. Acta*, *34*, 539 (1951).
711. Buu-Hoï and Hoán, *J. Org. Chem.*, *16*, 874 (1951).
712 Schomaker, *Acta Crystallog.*, *4*, 158 (1951).
713. Sheets, *Derivatives of Thianaphthene*, *Microfilm Abstracts*, *10*, No. 2, 22-23 (1950).
714. Birch and McAllen, *J. Inst. Petroleum*, *37*, 443 (1951).
715. Challenger and Emmott, *J. Inst. Petroleum*, *37*, 396 (1951).
716. Duffin and Kendall, *J. Chem. Soc.*, *1951*, 734.
717. Buu-Hoï, Hoán, and Jacquignon, *J. Chem. Soc.*, *1951*, 1381.
718. Illingworth and Peters, *J. Chem. Soc.*, *1951*, 1602.
719. Mustafa and Islam, *J. Chem. Soc.*, *1951*, 1616.
720. Illingworth and Peters, *J. Chem. Soc.*, *1951*, 2508.
721. Emerson, *J. Am. Chem. Soc.*, *73*, 1854 (1951).
722. Bordwell and McKellin, *J. Am. Chem. Soc.*, *73*, 2251 (1951).
723. Schonberg and Mustafa, *J. Am. Chem. Soc.*, *73*, 2401 (1951).
724. Schlesinger and Mowry, *J. Am. Chem. Soc.*, *73*, 2614 (1951).
725. Schonberg, Mustafa, and Asker, *J. Am. Chem. Soc.*, *73*, 2876 (1951).
726. Gould and McCullough, *J. Am. Chem. Soc.*, *73*, 3196 (1951).
727. Maginnity and Gaulin, *J. Am. Chem. Soc.*, *73*, 3579 (1951).
728. Brode and Wyman, *J. Am. Chem. Soc.*, *73*, 4267 (1951).
729. Burckhalter and Sam, *J. Am. Chem. Soc.*, *73*, 4460 (1951).
730. Barkley and Levine, *J. Am. Chem. Soc.*, *73*, 4625 (1951).
731. Gilman and Ingham, *J. Am. Chem. Soc.*, *73*, 4982 (1951).
732. Brooker *et al.*, *J. Am. Chem. Soc.*, *73*, 5326 (1951).
733. Bordwell, McKellin, and Babcock, *J. Am. Chem. Soc.*, *73*, 5566 (1951).
734. Illuminati, Nobis, and Gilman, *J. Am. Chem. Soc.*, *73*, 5887 (1951).
735. Gilman and Esmay, *J. Am. Chem. Soc.*, *74*, 266 (1952).
736. Shirley and Cameron, *J. Am. Chem. Soc.*, *74*, 664 (1952).
737. Gaertner, *J. Am. Chem. Soc.*, *74*, 766 (1952).
738. Truce and Milionis, *J. Am. Chem. Soc.*, *74*, 974 (1952).
739. Gilman and Lentz, *J. Am. Chem. Soc.*, *74*, 1107 (1952).
740. Brown, Nelson, and Wood, *J. Am. Chem. Soc.*, *74*, 1165 (1952).
741. Buu-Hoï and Hoán, *J. Chem. Soc.*, *1951*, 251.
742. Montgomery and Smith, *J. Chem. Soc.*, *1952*, 258.
743. Cagniant and Cagniant, *Compt. rend.*, *232*, 238 (1951).
744. Finke, Gross, Messerly, and Waddington, U. S. Bureau of Mines, Bartlesville, Okla., unpublished material APIRP 48A.
745. Sakan *et al.*, *J. Inst. Polytech.*, *Osaka City Univ.*, *1*, No. 2, 31 (1950); *Chem. Abstracts*, *46*, 2047 (1952).
746. Chapman, *M.S. dissertation*, Northwestern University, 1951.
747. Stange, *Ph.D. dissertation*, Northwestern University, 1950.
748. Lampert, *Ph.D. dissertation*, Northwestern University, 1951.
749. Martynoff, *Compt. rend.*, *234*, 736 (1952).
750. Buu-Hoï and Jacquignon, *Compt. rend.*, *234*, 1056 (1952).
751. Parham, Gordon, and Swalen, *J. Am. Chem. Soc.*, *74*, 1825 (1952).
751a. Baddely, *J. Chem. Soc.*, *1950*, 663.

752. Weinmayr, *J. Am. Chem. Soc.*, in press.
753. Schroeder and Weinmayr, *J. Am. Chem. Soc.*, in press.
754. Weinmayr, Palmer, and Ebert, *J. Am. Chem. Soc.*, in press.
755. Gilman and Esmay, *J. Am. Chem. Soc.*, *74*, 2021 (1952).
756. Kloosterziel and Backer, *Rec. trav. chim.*, *71*, 361 (1952).
757. Challenger, Fishwick, and Holmes, *private communication.*
758. Kosak and Selwitz, *private communication.*
759. Gaertner, *J. Am. Chem. Soc.*, *74*, 2185 (1952).
760. Brode and Wyman, *J. Research Natl. Bur. Standards*, *47*, 170 (1951).
761. Tilak, *Proc. Indian Acad. Sci.*, *32*, Sect. A, 390 (1950).
762. Sunthankar and Tilak, *Proc. Indian Acad. Sci.*, *32*, Sect. A., 396 (1950).
763. Sunthankar and Tilak, *Proc. Indian Acad. Sci.*, *33*, Sect. A, 35 (1951).
764. Tilak, *Proc. Indian Acad. Sci.*, *33*, Sect. A, 71 (1951).
765. Dikshit and Tilak, *Proc. Indian Acad. Sci.*, *33*, Sect. A, 78 (1951).
766. Tilak, *Proc. Indian Acad. Sci.*, *33*, Sect. A, 85 (1951).
767. Rabindran and Tilak, *Current Science*, *20*, 205 (1951).
768. Rabindran and Tilak, *Current Science*, *20*, 207 (1951).
769. Price and Hydock, *J. Am. Chem. Soc.*, *74*, 1945 (1952).
770. Roberts, Webb, and McElhill, *J. Am. Chem. Soc.*, *72*, 408 (1950).
771. Sheehan and Leitner, *J. Am. Chem. Soc.*, *74*, 5501 (1952).
772. Sheehan, *J. Am. Chem. Soc.*, *74*, 5505 (1952).
773. Sawicki and Ray, *J. Am. Chem. Soc.*, *74*, 4120 (1952).
774. Buu-Hoï and Hoán, *J. Chem. Soc.*, *1952*, 3745.
775. Buu-Hoï and Hoán, *J. Org. Chem.*, *17*, 643 (1952).
776. Gaertner, *J. Am. Chem. Soc.*, *74*, 4950 (1952).
777. Shirley and Danzig, *J. Am. Chem. Soc.*, *74*, 2935 (1952).
778 Cagniant and Cagniant, *Bull. soc. chim. France*, *1952*, 336.
779. Gilman and Esmay, *J. Am. Chem. Soc.*, *75*, 278 (1953).
780. Guha and Sinha, *J. Ind. Chem. Soc.*, *29*, 415 (1952).
781. Goncalves, Kegelman, and Brown, *J. Org. Chem*, *17*, 705 (1952).
782. Cagniant and Cagniant, *Bull. soc. chim. France*, *1952*, 629.
783. Davies, Gamble, James, and Savige, *Chem. and Ind.*, *1952*, 804.
784. Davies, Gamble, and Savige, *J. Chem. Soc.*, *1952*, 4678.

Patent Bibliography

P-1. Brit. Pat., 11,173 (1906); *Chem. Abstracts*, *1*, 1792 (1907).
P-1a. Ger. Pat., 188,702 (1905); *Chem. Abstracts*, *2*, 1207 (1908).
P-2. Brit. Pat., 11,479 (1906); *Chem. Abstracts*, *1*, 1923 (1907).
P-3. Brit. Pat., 14,192 (1906); *Chem. Abstracts*, *1*, 1924 (1907).
P-4. Brit. Pat., 14,507 (1906); *Chem. Abstracts*, *1*, 1194 (1907).
P-4a. Brit. Pat., 17,559 (1906); *Chem. Abstracts*, *1*, 1926 (1907).
P-5. Brit. Pat., 26,190 (1906); *Chem. Abstracts*, *1*, 2838 (1907).
P-6. Brit. Pat., 1,592 (1907); *Chem. Abstracts*, *2*, 485 (1908).
P-7. Brit. Pat., 4,592 (1907); *Chem. Abstracts*, *2*, 2017 (1908).
P-8. Brit. Pat., 10,541 (1907); *Chem. Abstracts*, *2*, 1763 (1908).
P-9. Brit. Pat., 11,609 (1907); *Chem. Abstracts*, *2*, 488 (1908).
P-10. Brit. Pat., 14,846 (1907); *Chem. Abstracts*, *2*, 2161 (1908).
P-11. Brit. Pat., 8,381 (1908); *Chem. Abstracts*, *3*, 1931 (1909).
P-12. Brit. Pat., 8,726 (1908); *Chem. Abstracts*, *3*, 2384 (1909).
P-13. Brit. Pat., 10,755 (1908); *Chem. Abstracts*, *3*, 2384 (1909).
P-14. Brit. Pat., 17,498 (1908); *Chem. Abstracts*, *3*, 2509 (1909).

P-15. Brit. Pat., 16,996 (1909); *Chem. Abstracts, 4*, 2579 (1910).

P-16. Brit. Pat., 18,117 (1909); *Chem. Abstracts, 5*, 2431 (1911)

P-17. Brit. Pat., 12,321 (1910); *Chem. Abstracts, 5*, 2963 (1911)

P-18. Brit. Pat., 16,517 (1910); *Chem. Abstracts, 5*, 3165 (1911).

P-19. Brit. Pat., 24,569 (1910); *Chem. Abstracts, 6*, 1532 (1912).

P-20. Brit. Pat., 2,732 (1911); *Chem. Abstracts, 6*, 1996 (1912).

P-21. Brit. Pat., 13,550 (1911); *Chem. Abstracts, 6*, 3528 (1912).

P-22. Brit. Pat., 18,589 (1911); *Chem. Abstracts, 7*, 420 (1913).

P-23. Brit. Pat., 21,988 (1911); *Chem. Abstracts, 7*, 1104 (1913).

P-25. Brit. Pat., 22,067 (1911); *Chem. Abstracts, 7*, 1104 (1913).

P-26. Brit. Pat., 186,057 (1922); *Centr., 1923*, II, 577.

P-27. Brit. Pat., 189,782 (1922); *Chem. Abstracts, 17*, 2509 (1923).

P-28. Brit. Pat., 186,859 (1921); *Chem. Abstracts, 17*, 1029 (1923).

P-29. Brit. Pat., 198,415 (1922); *Chem. Abstracts, 17*, 3793 (1923).

P-30. Brit. Pat., 202,734 (1922); *Chem. Abstracts, 18*, 333 (1924).

P-31. Brit. Pat., 209,092 (1923); *Chem. Abstracts, 18*, 1576 (1924).

P-32. Brit. Pat., 210,413 (1924); *Centr., 1924*, II, 1027.

P-33. Brit. Pat., 210,465 (1924); *Chem. Abstracts, 18*, 1673 (1924).

P-34. Imray, Brit Pat., 214,864 (1923); *Chem. Abstracts, 18*, 2813 (1924).

P-35. Brit. Pat., 214,864 (1923); *Centr., 1926*, I, 1299. Same as Swiss Pats. 105,397, 106,425 to 106,437, and 106,455 to 106,457 (1923).

P-36. Same as P-34; *Centr., 1926*, I, 1298.

P-37. Brit. Pat., 215,021 (1923); *Chem. Abstracts, 18*, 2967 (1924).

P-38. Brit. Pat., 216,347 (1923); *Chem. Abstracts, 19*, 77 (1925).

P-39. Brit. Pat., 218,014 (1923); *Chem. Abstracts, 19*, 524 (1925).

P-40. Brit. Pat., 219,280 (1923); *Chem. Abstracts, 19*, 578 (1925).

P-41. Brit. Pat., 221,418 (1923); *Chem. Abstracts, 19*, 899 (1925).

P-42. Brit. Pat., 222,094 (1923); *Chem. Abstracts, 19*, 1058 (1925). Same as Swiss 108,706 (1925).

P-43. Brit. Pat., 222,120 (1923); *Chem. Abstracts, 19*, 1058 (1925).

P-44. Brit. Pat., 226,373 (1923); *Centr., 1925*, I, 1914.

P-45. Brit. Pat., 231,567 (1924); *Chem. Abstracts, 19*, 3598 (1925).

P-46. Brit. Pat., 231,889 (1925); *Centr., 1925*, II, 1900.

P-49. Brit. Pat., 232,230 (1925); *Centr., 1925*, II, 2099.

P-50. Brit. Pat., 233,831 (1923); *Chem. Abstracts, 20*, 829 (1926).

P-51. Carpmael and Ransford, Brit. Pat., 234,928 (1924); *Chem. Abstracts, 20*, 992 (1926).

P-52. Brit. Pat., 235,252 (1924); *Chem. Abstracts, 20*, 992 (1926).

P-53. Brit. Pat., 235,252 (1924); *Chem. Abstracts, 20*, 992 (1926).

P-54. Brit. Pat., 235,277 (1924); *Chem. Abstracts, 20*, 992 (1926).

P-55. Brit. Pat., 235,877 (1924); *Chem. Abstracts, 20*, 992 (1926).

P-56. Brit. Pat., 236,332 (1924); *Chem. Abstracts, 20*, 992 (1926); *Centr., 1926*, I, 2976.

P-57. Brit. Pat., 246,156 (1925); *Chem. Abstracts, 21*, 415 (1927).

P-58. Brit. Pat., 249,489 (1925); *Chem. Abstracts, 21*, 1018 (1927).

P-59. Brit Pat., 251,293 (1926); *Centr., 1927*, I, 1231.

P-60. Dodd and Sprent, Brit. Pat., 251,637 (1925); *Chem. Abstracts, 21*, 1360 (1927).

P-61. Brit. Pat., 251,996 (1925); *Chem. Abstracts, 21*, 1553 (1927).

P-62. Brit. Pat., 254,310 (1925); *Chem. Abstracts, 21*, 2563 (1927).

P-63. Brit. Pat., 254,340 (1925); *Chem. Abstracts, 21*, 2479 (1927).

P-64. Brit. Pat., 254,743 (1926); *Centr., 1927*, I, 366.

P-65. Thomas, Harris, and Wylam, Brit. Pat., 258,626 (1926); *Centr.*, 1928, II, 1826. Same as Swiss 121,571.

P-66. Brit. Pat., 260,303 (1926); *Centr., 1927*, I, 1232.

-67. Brit. Pat., 260,940 (1925); *Chem. Abstracts, 21*, 3467 (1927).

-68. Brit. Pat., 261,383 (1927); *Centr., 1929*, I, 149.

-69. Brit. Pat., 262,457 (1925); *Chem. Abstracts, 21*, 3750 (1927).

-70. Brit. Pat., 265,193 (1927); *Centr., 1927*, II, 335.

-71. Brit. Pat., 266,382 (1926); *Chem Abstracts, 22*, 689 (1928).

-72. Brit. Pat., 267,177 (1927); *Centr., 1927*, II, 340.

-73. Brit. Pat., 271,906 (1926); *Chem. Abstracts, 22*, 1692 (1928).

-74. Brit Pat., 274,527 (1926); *Chem. Abstracts, 22*, 2277 (1928).

-75. Brit. Pat., 279,436 (1926); *Chem. Abstracts, 22*, 2846 (1928).

-76. Same as P-75.

-77. Brit. Pat., 279,489 (1926); *Chem. Abstracts, 22*, 2845 (1928); *Centr., 1928*, I, 759.

-78. Brit. Pat., 281,213 (1927); *Centr., 1928*, I, 1722.

-79. Brit. Pat., 282,805 (1928); *Centr., 1928*, I, 2012.

-80. Brit. Pat., 283,118 (1928); *Centr., 1928*, I, 2013.

-81. Brit. Pat., 284,288 (1928); *Centr., 1928*, I, 2132.

-82. Ellis, Brit. Pat., 284,376 (1928); *Centr., 1928*, I, 2543.

-83. Brit. Pat., 284,652 (1928); *Centr., 1928*, I, 2997.

-84. Brit. Pat., 285,389 (1927); *Chem. Abstracts, 22*, 4831 (1928).

-85. Brit. Pat., 286,369 (1928); *Centr., 1928*, II, 397.

-86. Brit. Pat., 288,215 (1927); *Chem. Abstracts, 23*, 714 (1929).

-87. Brit. Pat., 288,554 (1927); *Chem. Abstracts, 23*, 714 (1929).

-88. Brit. Pat., 288,986 (1927); *Chem. Abstracts, 23*, 715 (1929).

-89. Brit. Pat., 291,768 (1928); *Centr., 1928*, II, 2070.

-90. Brit. Pat., 292,622 (1928); *Centr., 1928*, II, 1948.

-91. Brit. Pat., 295,239 (1927); *Chem. Abstracts, 23*, 2302 (1929).

-92. Brit. Pat., 295,593 (1927); *Chem. Abstracts, 23*, 2304 (1929).

-92a. Brit. Pat., 295,694 (1927); *Chem. Abstracts, 23*, 2304 (1929).

-93. Brit. Pat., 296,761 (1927); *Chem. Abstracts, 23*, 2579 (1929).

-94. Brit. Pat , 298,493 (1929); *Centr., 1930*, I, 2011. Same as French Pat. 661,543 (1929).

-95. Brit. Pat., 300,114 (1927); *Chem. Abstracts, 23*, 3581 (1929).

-96. Brit. Pat., 302,175 (1927); *Chem. Abstracts, 23*, 4349 (1929).

-97. Brit. Pat., 304,794 (1928); *Chem. Abstracts, 23*, 4826 (1929).

-98. Brit. Pat., 309,379 (1928); *Chem. Abstracts, 24*, 731 (1930).

-99. Barns *et al.*, Brit. Pat., 309,970 (1929); *Centr., 1929*, II, 1354.

-100. Brit. Pat., 312,347 (1928); *Chem. Abstracts, 24*, 968 (1930); Addition to 297,376.

-101. Brit. Pat., 313,493 (1928); *Chem. Abstracts, 24*, 1226 (1930).

-102. Brit. Pat., 313,493 (1928); *Chem. Abstracts, 24*, 1226 (1930).

-103. Brit. Pat., 314,224 (1929); *Chem. Abstracts, 25*, 5038 (1931).

-104. Brit. Pat., 314,527 (1929); *Centr., 1930*, I, 130. Same as Ger. Pat., 504,248 (1930); *Centr., 1930*, II, 2840.

-105. Brit. Pat., 314,593 (1928); *Chem. Abstracts, 24*, 1520 (1930).

-106. Barnes, Harris, and Thomas, Brit. Pat., 317,736 (1929); *Centr., 1929*, II, 2734. Addition to 294,507.

-107. Brit. Pat., 318,595 (1929); *Centr., 1930*, I, 1383.

-108. Brit. Pat., 334,878 (1929); *Chem. Abstracts, 25*, 1394 (1931).

-108a. Brit. Pat., 334,919 (1929); *Chem. Abstracts, 25*, 1394 (1931).

-108b. Brit. Pat., 334,920 (1929); *Chem. Abstracts, 25*, 1394 (1931).

-108c. Brit. Pat., 338,104 (1930); *Chem. Abstracts, 25*, 2301 (1931).

-109. Brit. Pat., 341,224 (1931); *Centr., 1931*, I, 2684.

-110. Brit. Pat., 345,349 (1928); *Chem. Abstracts, 26*, 312 (1932).

-110a. Brit. Pat., 350,862 (1930); *Chem. Abstracts, 26*, 5429 (1932).

-111. Brit. Pat., 352,283 (1930); *Chem. Abstracts, 26*, 5427 (1932).

P-112. Brit. Pat. 354,716 (1931); *Centr., 1932*, II, 1084.

P-113. Brit. Pat., 355,597 (1929): *Chem. Abstracts, 26*, 5576 (1932).

P-114. Brit. Pat., 355,661 (1929); *Chem. Abstracts, 26*, 5767 (1932).

P-115. Brit. Pat., 355,662 (1929); *Chem. Abstracts, 26*, 5767 (1932).

P-116. Brit. Pat. 357,592 (1930); *Chem. Abstracts, 26*, 6149 (1932).

P-117. Brit. Pat., 357,593 (1930); *Chem. Abstracts, 27*, 195 (1933).

P-118. Brit. Pat., 359,426 (1929); *Chem. Abstracts, 27*, 426 (1933).

P-119. Brit. Pat., 360,349 (1931); *Chem. Abstracts, 27*, 515 (1933).

P-120. Brit. Pat., 360,533 (1930); *Chem. Abstracts, 27*, 1003 (1933).

P-121. Brit. Pat., 361,406 (1930); *Chem. Abstracts, 27*, 1196 (1933). Same as French Pat., 715,683; *Chem. Abstracts, 26*, 4722 (1932).

P-122. Brit. Pat., 368,505 (1930); *Chem. Abstracts, 27*, 2308 (1933).

P-123. Brit. Pat., 371,459 (1931); *Chem. Abstracts, 27*, 3086 (1933).

P-124. Brit. Pat., 373,601 (1932); *Chem. Abstracts, 27*, 4091 (1933). Same as French Pat., 726,110; *Chem. Abstracts, 26*, 4961 (1932).

P-125. Same as P-124.

P-126. Brit. Pat., 380,020 (1932); *Centr., 1932*, II, 3633.

P-127. Brit. Pat., 383,543 (1932); *Chem. Abstracts, 27*, 4411 (1933).

P-128. Brit. Pat., 383,662 (1932); *Chem. Abstracts, 27*, 4411 (1933).

P-129. Brit. Pat., 387,121 (1933); *Centr., 1933*, I, 2876.

P-130. Brit. Pat., 389,350 (1933); *Chem. Abstracts, 27*, 4683 (1933); *Centr., 1933*, I, 3799. Addition to 372,640 (*Chem. Abstracts, 27*, 3618 (1933)). Same as Ger. Pat., 552,927 (*Chem. Abstracts, 26*, 5767 (1933)).

P-131. Brit. Pat., 390,081 (1933); *Centr., 1933*, II, 2901.

P-132. Brit. Pat., 396,011 (1933); *Chem. Abstracts, 28*, 494 (1934). Same as Ger. Pat., 601,505.

P-133. Brit. Pat., 396,636 (1933); *Chem. Abstracts, 28*, 653 (1934).

P-134. Lodge and Lumsden, Brit. Pat., 398,161 (1933); *Chem. Abstracts, 28*, 1199 (1934).

P-135. Brit. Pat., 402,265 (1933); *Chem. Abstracts, 28*, 3242 (1934).

P-136. Brit. Pat., 407,578 (1934); *Chem. Abstracts, 28*, 5251 (1934). See also Swiss Pat. 163,279, 163,047 and 163,048 (*Chem. Abstracts, 28*, 2917 (1934)) and French Pat. 758,261 (1934) (*Chem. Abstracts, 28*, 3242 (1934)).

P-137. Brit. Pat., 409,014 (1934); *Centr., 1934*, II, 3050.

P-138. Brit. Pat., 418,561 (1934); *Centr., 1935*, I, 1963.

P-139. Brit. Pat., 422,606 (1935); *Centr., 1935*, II, 130.

P-140. Brit. Pat., 422,690 (1935); *Chem. Abstracts, 29*, 4598 (1935).

P-141. Brit. Pat., 431,661 (1935); *Chem. Abstracts, 29*, 8355 (1935).

P-142. Brit. Pat., 441,548 (1936); *Chem. Abstracts, 30*, 4685 (1936).

P-143. Brit. Pat., 442,167 (1936); *Chem. Abstracts, 30*, 4685 (1936).

P-144. Brit. Pat., 442,185 (1936); *Chem. Abstracts, 30*, 4684 (1936).

P-145. Brit. Pat., 458,405 (1937); *Centr., 1937*, II, 293.

P-146. Brit. Pat., 462,820 (1937); *Centr., 1937*, II, 3423.

P-147. Brit. Pat., 467,447 (1937); *Chem. Abstracts, 31*, 8213 (1937).

P-148. Brit. Pat., 468,640 (1937); *Chem. Abstracts, 32*, 801 (1938).

P-149. Brit. Pat., 471,488 (1938); *Centr., 1938*, II, 3269.

P-150. Brit. Pat., 485,964 (1938); *Chem. Abstracts, 32*, 8154 (1938).

P-151. Brit. Pat., 532,822 (1941); *Chem. Abstracts, 36*, 1045 (1942).

P-152. Brit. Pat., 541,097 (1941); *Chem. Abstracts, 36*, 4716 (1942).

P-153. Brit. Pat., 586,807 (1947); *Chem. Abstracts, 42*, 7991 (1948).

P-154. Brit. Pat., 607,608 (1948); *Chem. Abstracts, 43*, 9470 (1949).

P-155. Wilkinson, Brit. Pat., 619,357 (1949); *Chem. Abstracts, 43*, 8173 (1949). Same as U. S. Pat., 2,472,356 (1949).

P-156. Same as 155.

P-157. Brit. Pat., 1,099 (1884); *Ber. Referate*, *18*, 89 (1885).
P-158. French Pat., 366,875 (1906); *Chem. Abstracts*, *2*, 210 (1908).
P-159. French Pat., 367,739 (1906); *Chem. Abstracts*, *2*, 2869 (1908).
P-160. French Pat., 368,775 (1906); *Chem. Abstracts*, *2*, 2869 (1908).
P-160a. French Pat., 373,513 (1906); *Chem. Abstracts*, *2*, 2869 (1908).
P-161. French Pat., 372,627 (1909); *Chem. Abstracts*, *6*, 1997 (1912).
P-162. French Pat., 374,286 (1907); *Chem. Abstracts*, *2*, 2869 (1908).
P-162a. French Pat., 374,287 (1907); *Chem. Abstracts*, *3*, 2231 (1909).
P-163. French Pat., 377,540 (1907); *Chem. Abstracts*, *2*, 3288 (1908).
P-164. French Pat., 378,406 (1907); *Chem. Abstracts*, *2*, 3288 (1908).
P-165. French Pat., 383,927 (1907); *Chem. Abstracts*, *2*, 3409 (1908).
P-165a. French Pat., 384,381 (1907); *Chem. Abstracts*, *2*, 3410 (1908).
P-166. French Pat., 384,343 (1907); *Chem. Abstracts*, *2*, 3410 (1908).
P-167. French Pat., 384,418 (1907); *Chem. Abstracts*, *2*, 3410 (1908).
P-167a. French Pat., 384,532 (1907); *Chem. Abstracts*, *2*, 3410 (1908).
P-167b. French Pat., 384,606 (1907); *Chem. Abstracts*, *2*, 3410 (1908).
P-168. French Pat., 389,649 (1907); *Chem. Abstracts*, *3*, 2234 (1909).
P-169. French Pat., 407,228 (1909); *Chem. Abstracts*, *5*, 2965 (1911).
P-170. French Pat., 414,767 (1909); *Chem. Abstracts*, *6*, 1988 (1912).
P-171. French Pat., 421,574 (1910); *Chem. Abstracts*, *6*, 2005 (1912).
P-172. French Pat., 462,079 (1913); *Chem. Abstracts*, *8*, 2488 (1914).
P-173. French Pat., 576,103 (1924); *Centr.*, *1925*, I, 1915. Same as Swiss Pat., 106,465 to 106,468, 103,649, 106,469, 103,650, and 103,648.
P-174. French Pat., 576,876 (1924); *Centr.*, *1928*, II, 1827.
P-175. French Pat., 614,959 (1926); *Centr.*, *1929*, II, 797. Same as Brit. Pat., 251,270.
P-176. French Pat., 623,642 (1927); *Centr.*, *1928*, I, 420.
P-177. French Pat., 634,198 (1927); *Chem. Abstracts*, *22*, 3785 (1928).
P-178. French Pat., 635,255 (1928); *Centr.*, *1928*, I, 3119.
P-179. French Pat., 636,223 (1928); *Centr.*, *1929*, II, 1079. Same as Swiss Pat., 129,305 and Brit. Pat., 299,899.
P-180. French Pat., 642,906 (1927); *Chem. Abstracts*, *23*, 1511 (1929).
P-181. French Pat., 646,349 (1927); *Chem. Abstracts*, *23*, 2302 (1929).
P-182. French Pat., 648,069 (1928); *Chem. Abstracts*, *23*, 2446 (1929).
P-183. French Pat., 648,633 (1928); *Chem. Abstracts*, *23*, 2832 (1929).
P-184. French Pat., 652,049 (1928); *Chem. Abstracts*, *23*, 3477 (1929).
P-185. French Pat., 654,943 (1928); *Chem. Abstracts*, *23*, 3816 (1929).
P-186. French Pat., 658,850 (1928); *Chem. Abstracts*, *23*, 5194 (1929).
P-187. French Pat., 659,073 (1929); *Centr.*, *1930*, I, 2969.
P-188. French Pat., 661,348 (1928); *Chem. Abstracts*, *24*, 379 (1930).
P-189. Same as P-188.
P-190. French Pat., 661,543 (1928); *Chem. Abstracts*, *24*, 379 (1930).
P-191. Same as P-190.
P-192. French Pat., 664,911 (1928); *Chem. Abstracts*, *24*, 867 (1930).
P-193. French Pat., 665,356 (1929); *Centr.*, *1929*, II, 2833.
P-194. French Pat., 667,845 (1929); *Chem. Abstracts*, *24*, 1520 (1930).
P-195. French Pat., 675,725 (1929); *Chem. Abstracts*, *24*, 2894 (1930).
P-196. French Pat., 687,061 (1930); *Centr.*, *1931*, I, 692.
P-197. French Pat., 689,230 (1930); *Centr.*, *1930*, II, 3863.
P-198. French Pat., 693,303 (1930); *Centr.*, *1931*, I, 2944.
P-199. French Pat., 693,904 (1930); *Chem. Abstracts*, *25*, 2007 (1931). Same as Brit. Pat., 334,878 (1929).
P-200. French Pat., 693,996 (1930); *Centr.*, *1931*, I, 1975.
P-201. French Pat., 695,763 (1930); *Chem. Abstracts*, *25*, 2858 (1931)

P-202. French Pat., 695,979 (1930), *Chem. Abstracts*, *25*, 2857 (1931).

P-203. French Pat., 698,345 (1931); *Centr.*, *1931*, I, 2944.

P-204. French Pat., 698,407 (1931); *Centr.*, *1931*, I, 2944.

P-205. French Pat., 698,856 (1930); *Chem. Abstracts*, *25*, 3493 (1931).

P-206. French Pat., 702,529 (1930); *Chem. Abstracts*, *25*, 4411 (1931).

P-207. French Pat., 702,767 (1930); *Chem. Abstracts*, *25*, 4411 (1931).

P-208. French Pat., 702,795 (1930); *Chem. Abstracts*, *25*, 4285 (1931).

P-209. French Pat., 705,387 (1930), *Chem. Abstracts*, *25*, 5177 (1931).

P-210. French Pat., 715,919 (1931); *Chem. Abstracts*, *26*, 2063 (1932).

P-211. French Pat., 718,113 (1931); *Chem. Abstracts*, *26*, 2871 (1932).

P-212. French Pat., 720,382 (1932); *Centr.*, *1932*, II, 2115.

P-213. French Pat., 720,405 (1931); *Centr.*, *1932*, II, 2379.

P-214. French Pat., 721,087 (1931); *Chem. Abstracts*, *26*, 4183 (1932).

P-215. French Pat., 721,137 (1932); *Centr.*, *1932*, II, 784.

P-216. French Pat., 721,249 (1932); *Centr.*, *1932*, II, 622.

P-217. French Pat., 726,110 (1931); *Chem. Abstracts*, *26*, 4961 (1932).

P-218. French Pat., 727,605 (1931); *Chem. Abstracts*, *26*, 5768 (1932).

P-219. French Pat., 727,756 (1932); *Centr.*, *1932*, II, 2378.

P-220. French Pat., 735,298 (1932); *Chem. Abstracts*, *27*, 1196 (1933). Same as Brit. Pat., 383,543.

P-221. French Pat., 740,945 (1933); *Centr.*, *1933*, I, 3370.

P-222. French Pat., 745,841 (1933); *Chem. Abstracts*, *27*, 4415 (1933).

P-223. French Pat., 748,473 (1933); *Chem. Abstracts*, *27*, 5550 (1933).

P-224. French Pat., 749,461 (1933); *Centr.*, *1934*, I, 953.

P-225. French Pat., 756,401 (1933); *Centr.*, *1934*, I, 2496.

P-226. French Pat., 756,080 (1934); *Centr.*, *1934*, I, 3400.

P-227. French Pat., 758,261 (1934); *Centr.*, *1934*, I, 3131.

P-228. French Pat., 765,744 (1934); *Centr.*, *1934*, II, 3052.

P-229. French Pat., 766,452 (1934); *Centr.*, *1934*, II, 3679.

P-230. French Pat., 768,052 (1934); *Chem. Abstracts*, *29*, 475 (1935).

P-231. French Pat., 774,286 (1934); *Chem. Abstracts*, *29*, 2367 (1935).

P-232. French Pat., 776,153 (1935); *Centr.*, *1935*, II, 131.

P-233. French Pat., 778,477 (1935); *Centr.*, *1935*, II, 2287. Same as Swiss Pat., 172,735 (1935).

P-234. French Pat., 778,795 (1935); *Chem. Abstracts*, *29*, 4953 (1935).

P-235. Mannes and Godowsky, French Pat., 781,168 (1935); *Centr.*, *1935*, II, 2326.

P-236. French Pat., 786,168 (1935); *Centr.*, *1936*, I, 896.

P-237. French Pat., 786,183 (1935); *Centr.*, *1936*, I, 896.

P-238. French Pat., 789,663 (1935); *Chem. Abstracts*, *30*, 2014 (1936).

P-239. French Pat., 791,635 (1935); *Centr.*, *1936*, I, 3025.

P-240. French Pat., 792,667 (1936); *Centr.*, *1936*, I, 4216.

P-241. French Pat., 793,894 (1936). *Chem. Abstracts*, *30*, 4685 (1936).

P-242. Same as P-241.

P-243. French Pat., 795,181 (1936); *Centr.*, *1936*, II, 247.

P-244. French Pat., 800,625 (1936); *Chem. Abstracts*, *30*, 8640 (1936).

P-245. French Pat., 803,813 (1936); *Chem. Abstracts*, *31*, 2833 (1937).

P-246. French Pat., 812,077 (1936); *Centr.*, *1937*, II, 1271.

P-247. French Pat., 814,092 (1937), *Chem. Abstracts*, *32*, 1478 (1938).

P-248. French Pat., 814,762 (1937); *Chem. Abstracts*, *32*, 1484 (1938).

P-249. French Pat., 815,025 (1937); *Chem. Abstracts*, *32*, 1479 (1938).

P-250. French Pat., 823,196 (1938); *Centr.*, *1938*, I, 3391. Same as Swiss Pat., 192,579.

P-251. Henecki, French Pat., 823,937 (1938); *Chem. Abstracts*, *32*, 4285 (1938). See also Ger. Pat., 657,118 and 658 400.

P-252. French Pat., 864,963 (1941); *Centr.*, *1942*, I, 682.
P-253. French Pat., 865,519 (1941); *Centr.*, *1941*, II, 2617.
P-254. French Pat., 30,822 (1926); *Centr.*, *1927*, I, 1227. Addn. to 576,103.
P-255. French Pat., 31,422 (1927); *Centr.*, *1927*, II, 340. Addn. to 576,103.
P-256. French Pat., 32,810 (1926); *Chem. Abstracts*, *23*, 287 (1929). Addn.to 584,237.
P-257. French Pat., 32,850 (1926); *Chem. Abstracts*, *23*, 287 (1929). Addn.to 265,272.
P-258. French Pat., 36,846 (1929); *Chem. Abstracts*, *25*, 974 (1931). Addn.to 652,049.
P-259. French Pat., 39,288 (1930); *Chem. Abstracts*, *26*, 2199 (1932). Addn.to 702,795.
P-260. French Pat., 45,824 (1936); *Centr.*, *1936*, I, 3919. Addn. to French Pat., 774,286.
P-261. French Pat., 48,226 (1937); *Centr.*, *1938*, I, 4002. Addn. to 793,722. Same as Can. Pat., 368,949.
P-262. French Pat., 48,964 (1938); *Chem. Abstracts*, *33*, 5199 (1939). Addn. to 793,894.
P-264. Ger. Pat., 25,954; *Ber. Referate*, *17*, 366 (1884).
P-265. Ger. Pat., 33,088; *Ber. Referate*, *18*, 723 (1885).
P-266. Ger. Pat., 49,139; *Ber. Referate*, *23*, 46 (1890).
P-267. Ger. Pat., 51,497; *Ber. Referate*, *23*, 441 (1890).
P-268. Ger. Pat., 182,260 (1905); *Centr.*, *1907*, II, 867.
P-269. Ger. Pat., 188,702 (1905); *Centr.*, *1908*, I, 72.
P-270. Ger. Pat., 190,291 (1906); *Centr.*, *1908*, I, 424.
P-271. Ger. Pat., 190,292 (1906); *Centr.*, *1907*, II, 2094.
P-271a. Ger. Pat., 190,293 (1906); *Centr.*, *1907*, II, 2095.
P-272. Ger. Pat., 190,674 (1906); *Centr.*, *1908*, I, 424.
P-273. Ger. Pat., 191,097 (1906); *Centr.*, *1907*, II, 2095.
P-273a. Ger. Pat., 191,098 (1906); *Centr.*, *1907*, II, 2096.
P-274. Ger. Pat., 192,075 (1905); *Chem. Abstracts*, *2*, 1637 (1908).
P-275. Ger. Pat., 193,724 (1906); *Centr.*, *1908*, I, 1011.
P-276. Ger. Pat., 194,237 (1905); *Centr.*, *1908*, I, 1116.
P-277. Ger. Pat., 194,254 (1906); *Centr.*, *1908*, I, 1116.
P-278. Ger. Pat., 196,016 (1905); *Centr.*, *1908*, I, 1436.
P-279. Ger. Pat., 196,349 (1907); *Chem. Abstracts*, *2*, 2305 (1908).
P-280. Ger. Pat., 196,501 (1906); *Chem. Abstracts*, *2*, 2305 (1908).
P-280a. Ger. Pat., 197,037 (1907); *Chem. Abstracts*, *2*, 2305 (1908).
P-281. Ger. Pat., 197,150 (1905); *Centr.*, *1908*, I, 1587.
P-282. Ger. Pat., 197,162 (1906); *Chem. Abstracts*, *2*, 2454 (1908).
P-283. Ger. Pat., 198,509 (1907); *Chem. Abstracts*, *2*, 2629 (1908).
P-284. Ger. Pat., 198,644 (1907); *Chem. Abstracts*, *2*, 2629 (1908).
P-285. Ger. Pat., 198,645 (1907); *Chem. Abstracts*, *2*, 2630 (1908).
P-286. Same as P-285.
P-287. Ger. Pat., 198,692 (1906); *Chem. Abstracts*, *2*, 2732 (1908).
P-288. Ger. Pat., 198,712 and 198,713 (1905); *Chem. Abstracts*, *2*, 2732 (1908). Addns. to 192,075 and 196,016, respectively.
P-288a. Same as P-278.
P-289. Ger. Pat., 199,492 (1906); *Chem. Abstracts*, *2*, 3153 (1908).
P-290. Ger. Pat., 199,551 (1906); *Chem. Abstracts*, *2*, 3001 (1908).
P-291. Ger. Pat., 200,200 (1906); *Chem. Abstracts*, *2*, 3155 (1908).
P-292. Ger. Pat., 200,351 (1906); *Centr.*, *1908*, II, 552.
P-293. Ger. Pat., 200,202 (1907); *Chem. Abstracts*, *2*, 3155 (1908).
P-294. Same as P-293.
P-294a. Same as P-292.
P-295. Same as P-292.
P-296. Ger. Pat., 200,428 (1906); *Chem. Abstracts*, *2*, 3411 (1908).
P-296a. Ger. Pat., 200,593 (1906); *Chem. Abstracts*, *2*, 3411 (1908).

P-297. Ger. Pat., 201,970 (1905); *Chem. Abstracts, 3,* 491 (1909). Addn. to Ger. Pat., 197,150.
P-298. Ger. Pat., 202,696 (1906); *Chem. Abstracts, 3,* 492 (1909). Addn. to Ger. Pat, 184,496. Previous addn. to 190,291 and 190,674.
P-299. Same as P-298.
P-300. Ger. Pat., 202,707 (1907); *Chem. Abstracts, 3,* 595 (1909).
P-300a. Ger. Pat., 202,708 (1907), *Chem. Abstracts, 3,* 595 (1909).
P-301. Ger. Pat., 203,029 (1907); *Chem. Abstracts, 3,* 723 (1909). Addn. to Ger. Pat., 198,644.
P-302. Ger. Pat., 204,763 (1908); *Centr., 1909,* I, 233. Addn. to Ger. Pat, 199,551.
P-303. Same as P-302.
P-304. Ger. Pat., 205,002 (1906); *Centr., 1909,* I, 604.
P-305. Ger. Pat., 205,324 (1907); *Centr., 1909,* I, 605.
P-306. Ger. Pat., 205,377 (1907); *Chem. Abstracts, 3,* 1694 (1909).
P-307. Same as P-306.
P-308. Ger. Pat., 208,343 (1907); *Chem. Abstracts, 3,* 2058 (1909).
P-309. Ger. Pat., 208,499 (1907); *Chem. Abstracts, 3,* 2059 (1909).
P-310. Ger. Pat., 208,698 (1906); *Chem. Abstracts, 3,* 2060 (1909). Addn. to 192,872.
P-311. Ger. Pat., 210,343 (1908); *Centr., 1909,* II, 81.
P-313. Ger. Pat., 212,782 (1906); *Centr., 1909,* II, 767.
P-314. Ger. Pat., 212,942 (1906); *Centr., 1909,* II, 1024.
P-315. Ger. Pat., 213,458 (1906); *Centr., 1909,* II, 1393.
P-316. Ger. Pat., 213,465 (1907); *Centr., 1909,* II, 1101.
P-317. Ger. Pat., 213,474 (1908), *Centr., 1909,* II, 1392.
P-318. Ger. Pat., 213,960 (1908); *Chem. Abstracts, 4,* 390 (1910).
P-319. Ger. Pat. 214,715 (1908); *Chem. Abstracts, 4,* 520 (1910)
P-320. Ger. Pat., 214,781 (1907); *Chem. Abstracts, 4,* 520 (1910). Addn. to 212,782 (1906).
P-321. Ger. Pat., 217,556 (1908); *Centr., 1910,* I, 488.
P-322. Ger. Pat., 218,992 (1908); *Chem. Abstracts, 4,* 2048 (1910).
P-323. Ger. Pat., 221,216 (1908); *Chem. Abstracts, 4,* 2739 (1910).
P-324. Ger. Pat., 221,465 (1907); *Chem. Abstracts, 4,* 2740 (1910). Addn. to 205,324.
P-325. Ger. Pat., 219,268 (1908); *Chem. Abstracts, 4,* 2048 (1910). Addn. to 213,465 (1907).
P-326. Ger. Pat., 221,529 (1908); *Chem. Abstracts, 4,* 2740 (1910).
P-327. Ger. Pat., 224,567 (1906); *Centr., 1910,* II, 607.
P-328. Same as P-327.
P-329. Ger. Pat., 225,132 (1907); *Chem. Abstracts, 5,* 592 (1911). Addn. to 191,097.
P-330. Ger. Pat., 225,242 (1907); *Chem. Abstracts, 5,* 1195 (1911). Addn. to 182,260.
P-331. Ger. Pat., 228,914 (1908); *Centr., 1911,* I, 103. Addn. to Ger. Pat., 224,567.
P-332. Same as P-331.
P-333. Ger. Pat., 229,267 (1909); *Centr., 1911,* I, 182.
P-334. Ger. Pat., 229,369 (1909); *Centr., 1911,* I, 176.
P-335. Ger. Pat., 230,306 (1907); *Chem. Abstracts, 5,* 2733 (1911).
P-336. Ger. Pat., 230,308 (1907); *Chem. Abstracts, 5,* 2733 (1911).
P-337. Ger. Pat., 230,641 (1910); *Chem. Abstracts, 5,* 2735 (1911).
P-338. Ger. Pat., 231,927 (1909); *Chem. Abstracts, 5,* 2737 (1911).
P-339. Ger. Pat., 232,069 (1909); *Chem. Abstracts, 5,* 2738 (1911).
P-340. Ger. Pat., 232,277 (1906); *Centr., 1911,* I, 1019. Addn. to Ger. Pat., 192,075.
P-341. Ger. Pat., 232,995 (1909); *Chem. Abstracts, 5,* 2740 (1911).
P-342. Ger. Pat., 233,473 (1910); *Chem. Abstracts, 5,* 2742 (1911). Addn. to Ger. Pat. 232,714.
P-343. Ger. Pat., 233,601 (1909); *Centr., 1911,* I, 1335.
P-344. Ger. Pat., 233,741 (1910); *Centr., 1911,* I, 1390.

P-345. Ger. Pat., 234,306 (1910); *Centr., 1911*, I, 1617.
P-346. Ger. Pat., 235,625 (1909); *Chem. Abstracts, 5*, 3500 (1911).
P-347. Same as P-346.
P-348. Ger. Pat., 237,395 (1907); *Chem. Abstracts, 6*, 1501 (1912).
P-349. Same as P-348.
P-349a. Ger. Pat., 240,805 (1907); *Centr., 1911*, II, 1665.
P-349b. Ger. Pat., 241,326 (1908); *Centr., 1911*, II, 1665.
P-349c. Ger. Pat., 258,099 (1908); *Centr., 1913*, I, 1376.
P-349d. Same as P-326.
P-349e. Ger. Pat., 224,205 (1908); *Centr., 1910*, II, 612.
P-349f. Ger. Pat., 234,058 (1910); *Centr., 1911*, I, 1471.
P-349g. Same as P-368
P-350. Ger. Pat., 237,680 (1906); *Chem. Abstracts, 6*, 1538 (1912).
P-351. Ger. Pat., 239,089 (1906); *Chem. Abstracts, 6*, 1683 (1912). Addn. to Ger. Pat., 237,680.
P-352. Ger. Pat., 239,090 (1906); *Chem. Abstracts, 6*, 1683 (1912).
P-353. Ger. Pat., 239,091 (1906); *Chem. Abstracts, 6*, 1683 (1912).
P-354. Ger. Pat., 239,092 (1906); *Chem. Abstracts, 6*, 1683 (1912).
P-355. Ger. Pat., 239,093 (1907); *Chem. Abstracts, 6*, 1683 (1912).
P-356. Ger. Pat., 239,094 (1907); *Chem. Abstracts, 6*, 1683 (1912).
P-357. Ger. Pat., 239,089 (1907); *Centr., 1911*, II, 1290.
P-358. Same as P-340.
P-359. Same as P-353.
P-360. Ger. Pat., 239,337 (1909); *Centr., 1911*, II, 1500.
P-361. Ger. Pat., 239,673 (1907); *Chem. Abstracts, 6*, 1683 (1912).
P-362. Ger. Pat., 239,674 (1910); *Centr., 1911*, II, 1501.
P-363. Ger. Pat., 239,916 (1910); *Centr., 1911*, II, 1566.
P-364. Ger. Pat., 240,118 (1910); *Centr., 1911*, II, 1567.
P-365. Ger. Pat., 240,805 (1907); *Chem. Abstracts, 6*, 2179 (1912). Addn. to Ger. Pat., 239,673.
P-366. Ger. Pat., 241,326 (1910); *Centr., 1912*, I, 101.
P-367. Ger. Pat., 241,327 (1910); *Chem. Abstracts, 6*, 2180 (1912).
P-368. Ger. Pat., 241,343 (1910); *Chem. Abstracts, 6*, 2180 (1912). Addn. to Ger. Pat., 198,644.
P-369. Ger. Pat., 241,623 (1910); *Chem. Abstracts, 6*, 2145 (1912).
P-370. Ger. Pat., 242,220 (1910); *Centr., 1912*, I, 306.
P-371. Ger. Pat., 242,461 (1909); *Chem. Abstracts, 6*, 2323 (1912). Addn. to Ger. Pat., 232,780.
P-372. Same as P-371.
P-373. Ger. Pat., 242,532 (1910); *Chem. Abstracts, 6*, 2323 (1912). Addn. to Ger. Pat., 237,368.
P-374. Ger. Pat., 242,997 (1907); *Chem. Abstracts, 7*, 900 (1913). Addn. to Ger. Pat., 237,680.
P-375. Ger. Pat., 242,998 (1907); *Chem. Abstracts, 7*, 900 (1913).
P-376. Ger. Pat., 243,536 (1908); *Centr., 1912*, I, 455.
P-377. Ger. Pat., 246,581 (1911); *Centr., 1912*, I, 1937.
P-378. Ger. Pat., 252,771 (1910); *Chem. Abstracts, 7*, 553 (1913).
P-379. Ger. Pat., 263,470 (1912); *Chem. Abstracts, 7*, 4080 (1913); Addn. to Ger. Pat., 259,145.
P-380. Ger. Pat., 270,334 (1913); *Centr., 1914*, I, 830.
P-381. Ger. Pat., 277,358 (1908); *Chem. Abstracts, 9*, 966 (1915). Addn. to Ger. Pat., 191,097.
P-382. Ger. Pat., 305,559 (1915); *Centr., 1919*, IV, 409.
P-383. Ger. Pat., 321,119 (1915); *Centr., 1919*, IV, 256.

P-384. Ger. Pat., 325,712 (1918); *Centr.*, 1919, IV, 561.
P-385. Lange, Widman and Wennerberg, Ger. Pat., 330,833 (1920); *Centr.*, *1921*, II, 265.
P-386. Ger. Pat., 333,156 (1920); *Centr.*, *1921*, II, 762.
P-387. Weissgerber and Kruber, Ger. Pat., 341,837 (1922); *Chem. Abstracts*, *16*, 3487 (1922).
P-388. Ger. Pat., 342,733 (1922); *Chem. Abstracts*, *17*, 1243 (1923).
P-389. Ger. Pat., 350,737 (1919); *Centr.*, *1922*, IV, 160.
P-390. Weissgerber, Ger. Pat., 353,932 (1921); *Centr.*, *1922*, IV, 499.
P-391. Schirmacher, Zahn, and Schutz, Ger. Pat., 362,551 (1920); *Centr.*, *1923*, II, 528.
P-392. Schmidt and Rose, Ger. Pat., 380,712 (1923); *Centr.*, *1923*, IV, 991. Same as French Pat., 552,675 and U. S. Pat., 1,444,277.
P-393. Spengler and Thuron, Ger. Pat., 386,889 (1922); *Centr.*, *1924*, I, 1449.
P-394. Ger. Pat., 400,630 (1921); *Centr.*, *1924*, II, 2559.
P-395. Bauer, Haller, and Herre, Ger. Pat., 403,053 (1924); *Centr.*, *1925*, I, 1246.
P-396. Herz and Müller, Ger. Pat., 414,084 (1925); *Centr.*, *1925*, II, 861. Addn. to Ger. Pat., 410,310.
P-397. Hoffa, Ger. Pat., 414,260 (1923); *Centr.*, *1925*, II, 773. Same as French Pat., 580,166 (1924).
P-398. Schönberg, Ger. Pat., 426,476 (1923); *Centr.*, *1926*, I, 2840.
P-399. Bader and Sunder, Ger. Pat., 430,509 (1924); *Centr.*, *1926*, II, 1203. See also Ger. Pat., 424,981.
P-400. Müller-Conradi *et al.*, Ger. Pat., 441,179 (1927); *Centr.*, *1927*, I, 2135.
P-401. Münch, Ger. Pat., 445,566 (1925); *Centr.*, *1927*, II, 873.
P-402. Schoeller and Schmidt, Ger. Pat., 459,361 (1926); *Centr.*, *1928*, I, 2992.
P-403. Hoffa, Ger. Pat., 464,087 (1928); *Chem. Abstracts*, *22*, 4130 (1928).
P-404. Heyna *el al.*, Ger. Pat., 469,342 (1926); *Chem. Abstracts*, *23*, 1282 (1929).
P-405. Ger. Pat., 481,598 (1923); *Chem. Abstracts*, *24*, 247 (1930). Addn. to Ger. Pat., 455,280.
P-406. Hoffa *et al.*, Ger. Pat., 483,232 (1925); *Chem. Abstracts*, *24*, 504 (1930).
P-407. Herz and Thiess, Ger. Pat., 483,233 (1925); *Chem. Abstracts*, *24*, 504 (1930). Same as U. S. Pat., 1,655,697.
P-408. Weissgerber *et al.*, Ger. Pat., 483,759 (1927); *Centr.*, *1929*, II, 3267.
P-409. Münch, Ger. Pat., 489,725 (1926); *Centr.*, *1930*, II, 821.
P-410. Hoffa and Heyna, Ger. Pat., 490,599 (1925); *Chem. Abstracts*, *24*, 2306 (1930). Addn. to Ger. Pat., 450,799.
P-411. Flemming and Klein, Ger. Pat., 490,716 (1925); *Centr.*, *1930*, I, 3356.
P-412. Ger. Pat., 494,597 (1926); *Chem. Abstracts*, *24*, 3517 (1930).
P-413. Finger, Ger. Pat., 494,949 (1926); *Centr.*, *1930*, I, 3614.
P-414. Ger. Pat., 495,448 (1927); *Chem. Abstracts*, *3251* (1930).
P-415. Mayer, Ger. Pat., 495,976 (1926); *Chem. Abstracts*, *24*, 3517 (1930).
P-416. Same as P-415.
P-417. Mayer, Ger. Pat., 499,745 (1926); *Chem. Abstracts*, *24*, 4523 (1930).
P-418. Hoffa and Heyna, Ger. Pat., 500,162 (1927); *Chem. Abstracts*, *24*, 4404 (1930).
P-419. Mayer, Ger. Pat., 504,248 (1928); *Chem. Abstracts*, *24*, 5507 (1930). Same as Brit. Pat., 314,527.
P-420. Schirmacher and Fischer, Ger. Pat., 505,159 (1927); *Chem. Abstracts*, *24*, 5769 (1930).
P-421. Mayer and Zahn, Ger. Pat., 512,237 (1927); *Centr.*, *1931*, I, 1173.
P-422. Runne *et al.*, Ger. Pat., 515,541 (1927); *Chem. Abstracts*, *25*, 2442 (1931).
P-423. Thiess *et al.*, Ger. Pat., 518,951 (1926); *Chem. Abstracts*, *25*, 3495 (1931).
P-424. Ger. Pat., 519,265 (1928); *Chem. Abstracts*, *25*, 2857 (1931).
P-425. Runne and E. Fischer, Ger. Pat., 519,747 (1929); *Chem. Abstracts*, *25*, 3495 (1931).

P-426. Ger. Pat., 521,476 (1928); *Chem. Abstracts*, *25*, 2857 (1931).
P-427. Krauss, Ger. Pat., 524,828 (1926); *Chem. Abstracts*, *25*, 4411 (1931).
P-428. Hoffa *et al.*, Ger. Pat., 521,051 (1926); *Chem. Abstracts*, *25*, 2856 (1931).
P-429. Herz and Brunner, Ger. Pat., 525,688 (1928); *Chem. Abstracts*, *25*, 4715 (1931).
P-430. Thiess *et al.*, Ger. Pat., 530,907 (1927); *Chem. Abstracts*, *26*, 314 (1932). Addn. to Ger. Pat., 518,951.
P-431. Meissner *et al.*, Ger. Pat., 532,256 (1929); *Chem. Abstracts*, *26*, 314 (1932).
P-432. Hoffa and Heyna, Ger. Pat., 533,151 (1927); *Chem. Abstracts*, *26*, 604 (1932). Same as Brit. Pat., 288,555.
P-433. Kalischer and Ritter, Ger. Pat., 533,341 (1929); *Chem. Abstracts*, *26*, 480 (1932). Same as French Pat., 702,795.
P-434. Kalischer and Ritter, Ger. Pat., 546,512 (1930); *Chem. Abstracts*, *26*, 3519 (1932). Addn. to Ger. Pat., 533,341 and 534,909.
P-435. Kalischer and Ritter, Ger. Pat., 534,911 (1929); *Chem. Abstracts*, *26*, 3519 (1932). Addn. to Ger. Pat., 533,341.
P-436. Kalischer and Ritter, Ger. Pat., 534,910 (1929); *Chem. Abstracts*, *26*, 3519 (1932). Addn. to Ger. Pat., 533,341.
P-437. Hoffa and Heyna, Ger. Pat., 533,796 (1927); *Chem. Abstracts*, *26*, 853 (1932).
P-438. Same as 434–436 and in addition Ger. Pat., 534,909 (1929); *Centr.*, *1931*, II, 3399. See also Brit. Pat., 349,080.
P-439. Mayer, Ger. Pat., 538,311 (1925); *Centr.*, *1932*, II, 1374.
P-440. Haller, Ger. Pat., 539,331 (1930); *Chem. Abstracts*, *26*, 1620 (1932).
P-441. Bauer *et al.*, Ger. Pat., 540,619 (1930); *Chem. Abstracts*, *27*, 849 (1933). Addn. to Ger. Pat. 538,315.
P-442. Bauer *et al.*, Ger. Pat., 538,315 (1930); *Centr.*, *1932*, II, 1084.
P-443. Hoffa and Heyna, Ger. Pat., 540,861 (1929); Chem. Abstracts, *26*, 2326 (1932).
P-444. Heyna, Ger. Pat., 540,862 (1929); *Chem. Abstracts*, *26*, 2327 (1932).
P-445. Hoffa *et al.*, Ger. Pat., 543,286 (1927); *Chem. Abstracts*, *26*, 2468 (1932).
P-446. Haller, Ger. Pat., 545,714 (1930); *Chem. Abstracts*, *26*, 3517 (1932). Addn. to Ger. Pat., 539,331.
P-447. Hoffa and Heyna, Ger. Pat., 546,005 (1926); *Chem. Abstracts*, *26*, 3385 (1932).
P-448. Thiess *et al.*, Ger. Pat., 546,006 (1928); *Chem. Abstracts*, *26*, 3385 (1932).
P-448a. Ritter, Ger. Pat., 546,512 (1930); *Chem. Abstracts*, *26*, 3519 (1932).
P-449. Steiger, Ger. Pat., 547,925 (1932); *Centr.*, *1932*, I, 3504. Same as Brit. Pat., 360,533.
P-450. Ger. Pat., 549,663 (1932); *Centr.*, *1932*, II, 297. Addn. to Ger. Pat., 548,226.
P-451. Berthold, Ger. Pat., 551,680 (1927); *Centr.*, *1932*, II, 3017.
P-452. Steiger and Albrecht, Ger. Pat., 558,237 (1930); *Chem. Abstracts*, *27*, 732 (1933).
P-453. Steiger and Albrecht, Ger. Pat., 559,524 (1931); *Chem. Abstracts*, *27*, 732 (1933). Addn. to Ger. Pat., 558,237.
P-454. Steiger and Albrecht, Ger. Pat., 564,823 (1930); *Chem. Abstracts*, *27*, 1196 (1933).
P-455. Hoffa and Müller, Ger. Pat., 568,670 (1927); *Centr.*, *1933*, II, 938.
P-456. Ger. Pat., 570,364 (1927); *Centr.*, *1932*, I, 4039.
P-457. Hoffa and Müller, Ger. Pat., 570,766 (1933); *Chem. Abstracts*, *27*, 4412 (1933).
P-458. Tschunkur and Himmer, Ger. Pat., 579,917 (1933); *Chem. Abstracts*, *28*, 1053 (1934).
P-459. Same as P-458.
P-460. Ger. Pat., 579,918 (1933); *Chem. Abstracts*, *28*, *910* (1934).
P-461. Ger. Pat., 582,614 (1931); *Centr.*, *1933*, II, 2754.
P-462. Ger. Pat., 582,852 (1933); *Chem. Abstracts*, *28*, 907 (1934).
P-463. Thiess and Meissner, Ger. Pat., 583,649 (1933); *Chem. Abstracts*, *28*, 1199 (1934). Same as Brit. Pat., 383,543.
P-464. Ger. Pat., 585,961 (1931); *Centr.*, *1934*, I, 470.

P-465. Muth *et al.*, Ger. Pat., 591,213 (1932); *Centr., 1934*, I, 2196.
P-466. Muth, Ger. Pat., 593,506 (1934); *Chem. Abstracts, 28*, 3422 (1934).
P-467. Zerweck and Schubert, Ger. Pat., 596,399 (1934); *Centr., 1934*, II, 852.
P-468. Thiess *et al.*, Ger. Pat., 599,915 (1934); *Centr., 1934*, II, 2607.
P-469. Ger. Pat., 601,505 (1934); *Centr., 1935*, I, 160.
P-470. Herz and Schubert, Ger. Pat., 601,721 (1934); *Chem. Abstracts, 28*, 7551 (1934).
P-471. Steiger and Brunner, Ger. Pat., 602,095 (1934); *Chem. Abstracts, 29*, 611 (1935)
P-472. Pützer and Muth, Ger. Pat., 606,350 (1934); *Chem. Abstracts, 29*, 1434 (1935).
P-473. Muth and Geist, Ger. Pat., 607,381 (1934); *Chem. Abstracts, 29*, 1997 (1935).
P-474. Ger. Pat., 614,396 (1935); *Chem. Abstracts, 29*, 5862 (1935).
P-475. Steiger and Albrecht, Ger. Pat., 617,726 (1935); *Centr., 1936*, I, 192.
P-476. Krauss and Hagenböcker, Ger. Pat., 622,761 (1935); *Chem. Abstracts, 30*, 4014 (1936).
P-477. Ger. Pat., 623,554 (1936); *Chem. Abstracts, 30*, 5801 (1936).
P-478. Krauss, Ger. Pat., 627,903 (1936); *Chem. Abstracts, 30*, 6213 (1936).
P-479. Krauss and Hagenböcker, Ger. Pat., 630,221 (1936); *Chem. Abstracts, 31*, 2016 (1937). Addn. to Ger. Pat., 622,761.
P-480. Krauss and Brunner, Ger. Pat., 633,836 (1936); *Chem. Abstracts, 31*, 550 (1937).
P-481. Steiger and Brunner, Ger. Pat., 634,041 (1936); *Chem. Abstracts, 30*, 8640 (1936).
P-482. Ger. Pat., 638,450 (1936); *Chem. Abstracts, 31*, 1221 (1937). Same as Brit. Pat., 407,578.
P-483. Zerweck and Korten, Ger. Pat., 639,509 (1936); *Chem. Abstracts, 31*, 3506 (1937). Addn. to Ger. Pat., 631,099.
P-484. Honold, Ger. Pat., 658,072 (1938); *Chem. Abstracts, 32*, 4797 (1938). Addn. to Ger. Pat., 650,057.
P-485. Heyna, Ger. Pat., 745,417 (1943); *Chem. Abstracts, 40*, 2006 (1946).
P-486. Albrecht, U. S. Pat., 874,649 (1907); *Chem. Abstracts, 2*, 1202 (1908).
P-487. Homolka and Welde, U. S. Pat., 889,010 (1908); *Chem. Abstracts, 2*, 2865 (1908).
P-488. Homolka and Welde, U. S. Pat., 894,004 (1908); *Chem. Abstracts, 2*, 2865 (1908).
P-489. Homolka and Welde, U. S. Pat., 894,005 (1908); *Chem. Abstracts, 2*, 2865 (1908).
P-490. Homolka and Welde, U. S. Pat. 894,006 (1908); *Chem. Abstracts, 2*, 2865 (1908).
P-491. Homolka, U. S. Pat., 889,010 (1908); *Chem. Abstracts, 2*, 2865 (1908).
P-491a. Grob, U. S. Pat., 891,690 (1908).
P-492. Grob, U. S. Pat., 893,499 (1908); *Chem. Abstracts, 2*, 2865 (1908).
P-493. Same as P-488.
P-494. Same as P-489.
P-495. Same as P-490.
P-496. Engli, U. S. Pat., 893,468 (1908); *Chem. Abstracts, 2*, 2865 (1908).
P-497. Münch, U. S. Pat., 910,839 (1909); *Chem. Abstracts, 3*, 1091 (1909).
P-497a. Homolka, U. S. Pat., 898,738 (1908); *Chem. Abstracts, 3*, 379 (1909).
P-498. Münch, U. S. Pat., 949,592 (1910); *Chem. Abstracts, 4*, 1106 (1910).
P-499. Schmidt and Thiess, U. S. Pat., 955,699 (1910); *Chem. Abstracts, 4*, 1685 (1910).
P-500. Schmidt and Bryk, U. S. Pat., 963,813 (1910); *Chem. Abstracts, 4*, 2737 (1910).
P-501. Elbel, U. S. Pat., 965,170 (1910); *Chem. Abstracts, 4*, 2738 (1910).
P-502. Bauer and Herre, U. S. Pat., 1,434,983 (1922); *Centr., 1923*, II, 578.
P-503. Tolber *et al.*, U. S. Pat., 1,492,054 (1923); *Centr., 1924*, II, 1406. Same as Swiss Pat., 105,233 (1922) and Brit. Pat., 216,347 (1923).
P-504. Herz-Müller, U. S. Pat., 1,498,913 (1924); *Chem. Abstracts, 18*, 3279 (1924).

P-505. Tolber, U. S. Pat., 1,513,074 (1924); *Chem. Abstracts, 19,* 77 (1925). Same as Swiss Pats., 106,121; 106,123–4; 106,130; 106,132–4; Brit. Pats. 210,465 and 219,276.

P-506. Same as 505.

P-507. Hoffa and Heyna, U. S. Pat., 1,537,928 (1925); *Centr., 1925,* II, 1900.

P-508. Dinwiddie, U. S. Pat., 1,558,252 (1925); *Centr., 1926,* I, 1890.

P-509. Joyce, U. S. Pat., 1,568,458 (1926); *Chem. Abstracts, 20,* 670 (1926).

P-510. Staudinger *et al.*, U. S. Pat., 1,586,013 (1926); *Chem. Abstracts, 20,* 2167 (1926)

P-511. Herz and Brunner, U. S. Pat., 1,590,685 (1926); *Chem. Abstracts, 20,* 3088 (1926).

P-512. Hoffa, U. S. Pat., 1,592,210 (1926); *Chem. Abstracts, 20,* 3240 (1926).

P-513. Stocker and Müller, U. S. Pat., 1,598,167 (1926); *Chem. Abstracts, 20,* 3460 (1926).

P-514. Herz and Müller, U. S. Pat., 1,623,410 (1926); *Chem. Abstracts, 21,* 1714 (1927).

P-515. Herz, U. S. Pat., 1,631,865 (1927); *Chem. Abstracts, 21,* 2564 (1927).

P-516. Thiess *et al.*, U. S. Pat., 1,632,252 (1927); *Chem. Abstracts, 21,* 2564 (1927).

P-517. Krauss, U. S. Pat., 1,650,139 (1927); *Centr., 1928,* I, 759.

P-518. E. Fischer *et al.*, U. S. Pat., 1,655,692 (1928); *Centr., 1928,* I, 3119.

P-519. Krauss, U. S. Pat., 1,691,660 (1928); *Centr., 1929,* I, 1750.

P-520. Haller, U. S. Pat., 1,709,977 (1929); *Chem. Abstracts, 23,* 2834 (1929).

P-521. Hoffa and Heyna, U. S. Pat., 1,709,982 (1929); *Chem. Abstracts, 23,* 2834 (1929).

P-522. Steiger *et al.*, U. S. Pat., 1,712,365 (1929); *Chem. Abstracts, 23,* 3235 (1929).

P-523. Mayer, U. S. Pat., 1,713,670 (1929); *Chem. Abstracts, 23,* 3583 (1929).

P-524. Hoffa and Luce, U. S. Pat., 1,733,548 (1929); *Chem. Abstracts, 24,* 378 (1930)

P-525. Schirmacher and Eishold, U. S. Pat., 1,755,667 (1930); *Chem. Abstracts, 24,* 2894 (1930).

P-526. Hoffa and Heyna, U. S. Pat., 1,762,817 (1930); *Chem. Abstracts, 24,* 3908 (1930).

P-527. Mayer and Zahn, U. S. Pat., 1,765,687 (1930); *Chem. Abstracts, 24,* 4056 (1930).

P-528. Runne *et al.*, U. S. Pat., 1,765,703 (1930); *Chem. Abstracts, 24,* 4057 (1930).

P-529. Luttringhaus *et al.*, U. S. Pat., 1,778,159 (1930); *Chem. Abstracts, 24,* 5767 (1930).

P-530. Hoffa and Müller, U. S. Pat., 1,785,813 (1930); *Chem. Abstracts, 25,* 973 (1931).

P-531. Schimacher, U. S. Pat., 1,790,843 (1931); *Chem. Abstracts, 25,* 1683 (1931). Same as Brit. Pat., 222,094.

P-532. Thiess *et al.*, U. S. Pat., 1,792,130 (1931); *Chem. Abstracts, 25,* 2004 (1931).

P-533. Lubs and Dimwiddie, U. S. Pat., 1,792,648 (1931); *Centr., 1931,* I, 2809.

P-535. Schirmacher and Fischer, U. S. Pat., 1,797,104 (1931); *Chem. Abstracts, 25,* 2441 (1931).

P-536. Stocker and Müller, U. S. Pat., 1,880,996 (1932); *Chem. Abstracts, 27,* 513. (1933).

P-537. Bauer, U. S. Pat., 1,801,713 (1931); *Chem. Abstracts, 25,* 3495 (1931).

P-538. Hoffa *et al.*, U. S. Pat., 1,804,872 (1931); *Chem. Abstracts, 25,* 3846 (1931).

P-539. Herz *et al.*, U. S. Pat., 1,811,316 (1931); *Chem. Abstracts, 25,* 5040 (1931).

P-540. Mayer, U. S. Pat., 1,809,207 (1931); *Chem. Abstracts, 25,* 4412 (1931).

P-541. Same as P-540.

P-542. Gubbelmann *et al.*, U. S. Pat., 1,821,705 (1931); *Chem. Abstracts, 25,* 5998 (1931).

P-543. Heyna, U. S. Pat., 1,822,967 (1931); *Chem. Abstracts, 26,* 913 (1932).

P-545. Bauer and Zeh, U. S. Pat., 1,826,721 (1931); *Chem. Abstracts, 26,* 605 (1932).

P-546. Bauer and Zeh, U. S. Pat., 1,826,720 (1931); *Chem. Abstracts, 26,* 605 (1932).

P-547. Lubs and Fox, U. S. Pat., 1,850,758 (1932); *Chem. Abstracts, 26,* 2873 (1932).

P-548. Steiger, U. S. Pat., 1,857,264 (1932); *Chem. Abstracts, 26,* 3934 (1932).

P-549. Herz *et al.*, U. S. Pat., 1,876,930 (1932); *Chem. Abstracts, 27,* 1199 (1933).

P-550. Herz *et al.*, U. S. Pat., 1,877,316 (1932); *Chem. Abstracts, 27,* 1200 (1933).
P-551. Hoffa and Heyna, U. S. Pat., 1,877,870 (1922); *Chem. Abstracts, 27,* 1196 (1933).
P-552. Ritter and Brunner, U. S. Pat., 1,877,973 (1932); *Chem. Abstracts, 27,* 1196 (1933).
P-553. Bauer *et al.*, U. S. Pat., 1,890,718 (1932); *Chem. Abstracts, 27,* 1764 (1933).
P-554. Haller, U. S. Pat., 1,913,484 (1933); *Chem. Abstracts, 27,* 4416 (1933). Same as Ger. Pat., 547,714.
P-555. Mayer, U. S. Pat., 1,914,445 (1933); *Chem. Abstracts, 27,* 4411 (1933).
P-556. Steiger and Brunner, U. S. Pat., 1,938,053 (1933); *Chem. Abstracts, 28,* 1198 (1934).
P-557. Steiger and Brunner, U. S. Pat., 1,938,054 (1933); *Chem. Abstracts, 28,* 1198 (1934).
P-558. Steiger, U. S. Pat., 1,945,923 (1934); *Chem. Abstracts, 28,* 2372 (1934).
P-559. Hoffa and Heyna, U. S. Pat., 1,959,474 (1934); *Chem. Abstracts, 28,* 4606 (1934).
P-560. Stocklin, U. S. Pat., 1,990,010 (1935); *Chem. Abstracts, 29,* 2367 (1935).
P-561. Hagenböcker and Brune, U. S. Pat., 1,945,484 (1934); *Chem. Abstracts, 28,* 2544 (1934).
P-562. Lubs and Cole, U. S. Pat., 2,000,033 (1935); *Chem. Abstracts, 29,* 4186 (1935).
P-563. Krauss and Brunner, U. S. Pat., 2,005,041 (1935); *Chem. Abstracts, 29,* 5281 (1935).
P-564. Müller and Stocker, U. S. Pat., 2,007,094 (1935); *Chem. Abstracts, 29,* 5670 (1935).
P-565. Hagenböcker and Brüne, U. S. Pat., 2,029,714 (1936); *Chem. Abstracts, 30,* 2014 (1936).
P-566. Herz and Brunner, U. S. Pat., 2,044,790 (1936); *Chem. Abstracts, 30,* 5800 (1936).
P-567. Kraus and Hagenböcker, U. S. Pat., 2,044,796 (1936); *Chem. Abstracts, 30,* 5801 (1936).
P-568. Kraus and Hagenböcker, U. S. Pat., 2,045,475–7 (1936); *Chem. Abstracts, 30,* 5808 (1936).
P-569. Lulek, U. S. Pat., 2,049,214 (1936); *Chem. Abstracts, 30,* 6578 (1936).
P-570. Cole, U. S. Pat., 2,061,186 (1936); *Centr., 1937,* I, 2879.
P-571. Lubs and Fox, U. S. Pat., 2,061,200 (1936); *Centr., 1937,* I, 2879.
P-572. Carleton and Mattison, U. S. Pat., 2,062,443 (1936); *Chem. Abstracts, 31,* 883 (1937).
P-573. Havas, U. S. Pat., 2,063,161 (1936); *Chem. Abstracts, 31,* 880 (1937).
P-574. Fröhlich, U. S. Pat., 2,080,862 (1936); *Centr., 1937,* II, 1459.
P-575. Havas, U. S. Pat., 2,094,595 (1937); *Chem. Abstracts, 31,* 8944 (1937).
P-576. Havas, U. S. Pat., 2,094,597 (1937); *Chem. Abstracts, 31,* 8944 (1937).
P-577. Havas, U. S. Pat., 2,095,596 (1937); *Centr., 1938,* I, 3270.
P-578. Lulek and Belcher, U. S. Pat., 2,097,860 (1937); *Centr., 1938,* I, 1669.
P-579. Same as P-578.
P-580. Henecka, U. S. Pat., 2,112,961 (1938); *Chem. Abstracts, 32,* 4177 (1938). Same as Ger. Pat., 657,118.
P-581. Havas, U. S. Pat., 2,127,483 (1938); *Chem. Abstracts, 32,* 8155 (1938).
P-582. Lodge and Lumsden, U. S. Pat., 2,129,014 (1938); *Chem. Abstracts, 32,* 8793 (1938).
P-583. Coleman and Zemba, U. S. Pat., 2,136,334 (1938); *Chem. Abstracts, 33,* 1346 (1939).
P-584. Fox, U. S. Pat., 2,136,427 (1938); *Chem. Abstracts, 33,* 1513 (1939).
P-585. Fox, U. S. Pat., 2,136,428 (1938); *Chem. Abstracts, 33,* 1513 (1939).
P-586. Moyle and Bass, U. S. Pat., 2,151,984 (1939); *Centr., 1939,* II, 732.

P-587. Sweet, U. S. Pat., 2,154,709 (1939); *Chem. Abstracts, 33,* 5673 (1939).
P-588. Muth, U. S. Pat., 2,157,796 (1939); *Chem. Abstracts, 33,* 6346 (1939).
P-589. Lubs and Johnson, U. S. Pat., 2,158,032 (1939); *Centr., 1939,* II, 3638.
P-590. Cole, U. S. Pat., 2,173,506 (1939); *Chem. Abstracts, 34,* 635 (1940).
P-591. Muth, U. S. Pat., 2,189,367 (1940); *Chem. Abstracts, 34,* 4283 (1940).
P-592. Stilmar, U. S. Pat., 2,217,849 (1940); *Chem. Abstracts, 35,* 1242 (1941).
P-593. Cole and Skiles, U. S. Pat., 2,228,753 (1941); *Chem. Abstracts, 35,* 3103 (1941).
P-594. Stilmar, U. S. Pat., 2,233,496 (1941); *Centr., 1941,* II, 2166.
P-595. Linch, U. S. Pat., 2,359,862 (1944); *Chem. Abstracts, 39,* 2077 (1944).
P-596. Dickey and McNally, U. S. Pat., 2,397,928 (1946); *Chem. Abstracts, 40,* 3613 (1946).
P-597. Lecker *et al.,* U. S. Pat., 2,403,266 (1946); *Chem. Abstracts, 40,* 6264 (1946).
P-598. Middleton and Dawson, U. S. Pat., 2,424,483 (1947); *Chem. Abstracts, 42,* 1141 (1948).
P-599. Lubs and Johnson, U. S. Pat., 2,158,032 (1939); *Chem. Abstracts, 33,* 6612 (1939).
P-600. Same as P-598.
P-601. Scalera, U. S. Pat., 2,441,512 (1948); *Chem. Abstracts, 42,* 7992 (1948).
P-602. Hoelzle and Kambli, U. S. Pat., 2,453,225 (1948); *Chem. Abstracts, 43,* 7706 (1949).
P-603. Weinmayr, U. S. Pat., 2,472,133 (1949).
P-604. Greensfelder and Moore, U. S. Pat., 2,478,914 (1949).
P-605. Richter and Fuller, U. S. Pat., 2,479,513 (1949).
P-606. Belcher and Mero, U. S. Pat., 2,480,109 (1949).
P-607. Belcher and Mero, U. S. Pat., 2,480,111 (1949).
P-608. Lee and Weinmayr, U. S. Pat., 2,480,746 (1949).
P-609. Staudinger, Swiss Pat., 92,486–9, 92,688 (1926); *Centr., 1923,* II, 573.
P-610. Same as P-609.
P-611. Swiss Pats., 102,033, 104,921–8 (1922), 106,135 (1923); *Centr., 1925,* II, 774.
P-612. Swiss Pats., 104,932 (1924); *Centr., 1928,* II, 496. Addn. to Swiss Pat., 100,705.
P-613. Swiss Pats., 105,150–3 (1924); *Centr., 1926,* I, 1890. Addn. to Swiss Pat., 100,705.
P-614. Swiss Pat., 105,656 (1924); *Centr., 1926,* I, 1890.
P-615. Swiss Pat., 106,120 (1924); *Centr., 1926,* I, 496.
P-616. Swiss Pat., 106,218 (1925); *Centr., 1926,* I, 1053.
P-619. Swiss Pat., 107,133–5 (1925); *Centr., 1925,* II, 860.
P-620. Swiss Pat., 108,703 (1924); *Centr., 1926,* I, 1299.
P-621. Bader and Sunder, Swiss Pat., 110,419 (1925); *Centr., 1926,* I, 1053.
P-622. Swiss Pat., 119,147 to 119,152 (1925); *Centr., 1927,* II, 870.
P-623. Bader and Sunder, Swiss Pat., 119,917 (1927); *Centr., 1927,* II, 1096.
P-624. Swiss Pat., 121,571 (1927), *Centr., 1928,* II, 813.
P-625. Bader and Sunder, Swiss Pat., 123,685 (1927); *Centr., 1928,* I, 1722.
P-626. Bader and Sunder, Swiss Pat., 126,969 to 126,973 (1926); *Centr., 1929,* I, 308 Addn. to Swiss Pat., 102,540.
P-627. Swiss Pat., 129,265 (1927); *Chem. Abstracts, 23,* 2832 (1929). Same as Brit. Pat., 292,741 and French Pat., 656,133.
P-628. Swiss Pat., 129,589 (1927); *Chem. Abstracts, 23,* 2833 (1929).
P-629. Swiss Pat., 130,083–7 (1929); *Centr., 1929,* II, 2736.
P-630. Swiss Pat., 134,093 (1927); *Chem. Abstracts, 24,* 1748 (1930).
P-631. Swiss Pat., 137,740 (1930); *Centr., 1930,* II, 3863.
P-632. Bader and Sunder, Swiss Pat., 138,243 (1928); *Chem. Abstracts, 25,* 821 (1931). Addn. to Swiss Pat., 102,540.
P-633. Same as P-632

P-634. Swiss Pat., 138,866, 140,574–6 (1930); *Centr., 1931,* I, 167.
P-635. Swiss Pat., 139,069 to 139,071 (1930); *Centr., 1931,* I, 167.
P-636. Bader and Sunder, Swiss Pat., 140,015–6 (1930); *Centr., 1930,* II, 3656. Addn. to Swiss Pat., 102,540.
P-637. Swiss Pat., 140,091 (1930); *Centr., 1931,* II, 770.
P-638. Swiss Pat., 153,835 (1931); *Chem. Abstracts, 27,* 1196 (1933).
P-639. Swiss Pat., 154,505 (1932); *Centr., 1933,* I, 1849. Same as Brit. Pat., 373,601.
P-640. Swiss Pat., 155,791 (1932); *Centr., 1933,* I, 1694.
P-641. Swiss Pat., 156,927 (1932); *Centr., 1933,* I, 1849.
P-642. Swiss Pat., 157,312 (1932); *Centr., 1933,* II, 285.
P-643. Swiss Pat., 158,240 (1933); *Chem. Abstracts, 27,* 4936 (1933).
P-644. Swiss Pat., 172,734 (1935); *Chem. Abstracts, 29,* 5666 (1935).
P-645. Swiss Pat., 183,677 (1936); *Centr., 1937,* I, 677.
P-646. Swiss Pat., 193,626 (1938); *Centr., 1938,* II, 2849.
P-647. Swiss Pat., 215,591–2 (1941); *Chem. Abstracts, 42,* 3970 (1948).
P-648. Chapiro and Gach, Belg. Pat., 390,439 (1932); *Chem. Abstracts, 27,* 2696 (1933).
P-649. Businger, Can. Pat., 433,566 (1946); *Chem. Abstracts, 40,* 3857 (1946).
P-650. Gubbelmann *et al.*, Can. Pat., 331,849 (1933); *Chem. Abstracts, 27,* 4091 (1933).
P-651. Glass *et al.*, Can. Pat., 436,212 (1946).
P-652. Lubs and Fox, Can. Pat., 340,405 (1934); *Centr., 1935,* I, 3716.
P-653. Czech. Pat., 31,135 (1930); *Centr., 1932,* I, 1582.
P-654. Asahina, Jap. Pat., 129,192 (1939); *Chem. Abstracts, 34,* 7936 (1940).
P-655. Polish Pat., 9,449 (1929); *Centr., 1929,* II, 2831.
P-656. Polish Pat., 8,819 (1928); *Centr., 1930,* II, 1915.
P-657. Kliger, Russ Pat., 52,346 (1938); *Centr., 1938,* II, 958.
P-658. Levkoev and Sveshnikov, Russ. Pat., 55,421 (1939); *Chem. Abstracts, 38,* 4619 (1944).
P-659. Levkoev and Sveshnikov, Russ. Pat., 58,099 (1940); *Chem. Abstracts, 38,* 5742 (1944).
P-660. Zaitzev, Russ. Pat., 50,849 (1937); *Chem. Abstracts, 33,* 4050 (1939).
P-661. Jerschow, Russ. Pat., 48,952 (1936); *Centr., 1937,* II, 477.
P-662. Willstaedt, Swed. Pat., 123,080 (1948); *Chem. Abstracts, 43,* 6662 (1949).
P-663. Lee and Weinmayr, U. S. Pat., 2,497,311 (1950).
P-664. Lee and Weinmayr, U. S. Pat., 2,497,312 (1950).
P-665. Weinmayr, U. S. Pat., 2,497,334 (1950).
P-666. Killian, U. S. Pat., 2,493,072 (1950).
P-667. Cheney and Peining, U. S. Pat., 2,466,004 (1949).
P-668. Flowers and Flowers, U. S. Pat., 2,499,186 (1950).
P-669. Ger. Pat., 38,795 (1887); *Ber. Referate, 20,* 272 (1887).
P-670. Lee and Weinmayr, U. S. Pat., 2,501,131 (1950).
P-670a. Lee and Weinmayr, U. S. Pat., 2,513,573 (1950).
P-671. Lee and Weinmayr, U. S. Pat., 2,501,132 (1950).
P-672. Cullinan and Lytle, U. S. Pat., 2,475,821 (1950).
P-673. Cheney, U. S. Pat., 2,502,422 (1950).
P-674. Hojima, Yamamuro, and Sahan, Jap. Pat., 175,175 (1947); *Chem. Abstracts 44,* 5913 (1950).
P-675. Belcher and Mero, U. S. Pat., 2,480,109–112 (1949); *Chem. Abstracts, 44,* 6152 (1950).
P-676. Patterson and Culnane, U. S. Pat. 2,509,938 (1950); *Chem. Abstracts, 44,* 8375 (1950).
P-677. Hamer and Knott, Brit., Pat., 593,023 (1947); *Chem. Abstracts, 43,* 513 (1949).
P-678. Lee and Weinmayr, U. S. Pat., 2,513,571 (1950).
P-678a. Lee and Weinmayr, U. S. Pat., 2,513,570 (1950).
P-679. Lee and Weinmayr, U. S. Pat., 2,513,574 (1950).
P-679a. Lee and Weinmayr, U. S. Pat., 2,513,572 (1950).

P-680. Feiser and Schroeder, U. S. Pat., 2,513,790 (1950).
P-681. Ger. Pat., 243,751; *Centr., 1912,* I, 867.
P-682. Schneider, U. S. Pat., 1,949,815 (1934); *Chem. Abstracts, 28,* 3084 (1934).
P-683. Brit. Pat., 502,320; *Chem. Abstracts, 33,* 6622 (1939).
P-684. Swiss Pat., 240,798 (1946); *Chem. Abstracts, 43,* 6427 (1949).
P-685. Swiss Pat., 243,514 (1947); *Chem. Abstracts, 43,* 5967 (1949). Addn. to 240,798.
P-686. Swiss Pat., 245,577 (1947); *Chem. Abstracts, 43,* 4867 (1949). Addn. to 240,798.
P-687. Swietoslawski and Anderson, U. S. Pat., 2,470,116 (1949); *Chem. Abstracts, 43,* 5236 (1949).
P-688. Mueller and Bavely, U. S. Pat., 2,449,244 (1948); *Chem. Abstracts, 43,* 513 (1949).
P-689. Avakian and Martin, U. S. Pat., 2,517,826 (1950).
P-690. Richter and Fuller, U. S. Pat., 2,528,785 (1950).
P-691. Richter and Fuller, U. S. Pat. 2,527,334 (1950).
P-692. Richter and Fuller, U. S. Pat., 2,527,335 (1950).
P-693. Wilkinson, Brit. Pat., 619,357; 633,478; 633,487; 633,492 (1949); *Chem. Abstracts, 45,* 1775 (1951).
P-694. Max and Schmidt-Nickels, U. S. Pat., 2,533,171 (1950); *Chem. Abstracts, 45,* 1775 (1951).
P-695. Amshutz, U. S. Pat., 2,529,860 (1950).
P-696. Schroeder and Ringrose, U. S. Pat., 2,559,670 (1951).
P-697. Schroeder and Ringrose, U. S. Pat., 2,559,671 (1951).
P-698. Schroeder and Ringrose, U. S. Pat., 2,559,672 (1951).
P-699. Schroeder and Ringrose, U. S. Pat., 2,559,673 (1951).
P-700. Schroeder and Ringrose, U. S. Pat., 2,559,674 (1951).
P-701. Schroeder and Ringrose, U. S. Pat., 2,559,677 (1951).
P-702. Lee and Weinmayr, U. S. Reissue 23,389 (1951); Reissue of U. S. Pat. 2,501,131.
P-703. Lee and Weinmayr, U. S. Reissue 23,390 (1951); Reissue of U. S. Pat. 2,501,132.
P-704. Devaney, U. S. Pat., 2,537,446 (1951); *Chem. Abstracts, 45,* 4745 (1951).
P-705. Martin and Avakian, U. S. Pat., 2,550,017 (1951).
P-706. Avakian and Martin, U. S. Pat., 2,553,495 (1951); *Chem. Abstracts, 46,* 537 (1952).
P-707. Van Vleck, U. S. Pat., 2,557,708 (1951); *Chem. Abstracts, 46,* 537 (1952).
P-708. Richter and Fuller, U. S. Pat., 2,571,384 (1951); *Chem. Abstracts, 46,* 731 (1952).
P-709. Scalera and Forster, U. S. Pat., 2,573,652 (1951).
P-710. Long and Tsang, U. S. Pat., 2,590,632 (1952).
P-711. Scalera and Eberhart, U. S. Pat., 2,563,493 (1951).
P-712. Scalera and Eberhart, U. S. Pat., 2,563,795 (1951).
P-713. Swiss Pat., 251,880 (1948); *Chem. Abstracts, 44,* 6155 (1950).

RING INDEX

Arranged according to progression in Patterson's *Ring Index.* See *Subject Index for page numbers.*

2-Ring Systems

4,5	C_2OS-C_4S	Oxathiabicyclohexane
	$C_2S_2-C_4S$	Dithiabicyclohexane
5,5	$C_2OS_2-C_4S$	Thienooxadithiole
	C_3NO-C_4S	Thienooxazole
	$C_3N_2-C_4S$	Thienopyrazole
		Thienoimidazole
	C_4N-C_4S	Thienopyrrole
	C_4O-C_4S	Thienofuran (2 isomers)
	C_4S-C_4S	Thienothiophene (3 isomers)
	C_4Se-C_4Se	Selenophenoselenophene (3 isomers)
	C_4S-C_5	Cyclopenta[*b*]thiophene
5,6	$C_4S-C_4O_2$	Thieno-*p*-dioxin
	C_4S-C_5O	Thienopyran (2 isomers)
	C_4S-C_5S	Thienothiapyran (2 isomers)
	C_4S-C_5N	Thienopyridine (5 isomers)
	C_4S-C_6	Thianaphthene
		Isothianaphthene
	C_4Se-C_6	Selenonaphthene
		Isoselenonaphthene
	C_4Te-C_6	Telluronaphthene
5,7	C_4S-C_7	Cyclohepta[*b*]thiophene

3-Ring Systems

5,5,6	$C_2N_3-C_4S-C_6$	Thianaphthenotriazole
	$C_3NS-C_4S-C_6$	Thianaphthenothiazole (4 isomers)
	$C_3N_2-C_4S-C_6$	Thienoindazole (2 isomers)
		Thianaphthenopyrazole
	$C_3O_2-C_4S-C_6$	Thianaphthenedioxole (2 isomers)
	$C_4N-C_4S-C_6$	Thienoindole
		Thianaphthenopyrrole
	$C_4O-C_4S-C_6$	Furothianaphthene
	$C_4S-C_4S-C_4Hg_2$	Dithieno-*p*-dimercurin
	$C_4S-C_4S-C_5S$	Dithienothiapyran
	$C_4S-C_4S-C_6$	Thienothianaphthene
		Benzodithiophene (3 isomers)
		1,4-Thionaphthalene
	$C_4S-C_5-C_6$	Indenothiophene
		Cyclopentathianaphthene

3-Ring Systems (continued)

5,5,8	$C_4S-C_4S-C_4S_2Hg_2$	Dithiodimercurecin
5,6,6,	$C_4S-C_4NO-C_6$	Thianaphthenooxazine (2 isomers)
	$C_4S-C_4NS-C_6$	Thianaphthenothiazine (2 isomers)
	$C_4S-C_4N_2-C_6$	Thianaphthenopyridazine
		Thienocinnoline
		Thianaphthenopyrimidine
		Thianaphthenopyrazine
	$C_4S-C_5N-C_6$	Thienoquinoline (5 isomers)
		Thianaphthenopyridine
	$C_4S-C_5O-C_6$	Pyranothianaphthene (3 isomers)
		Benzothienopyran (2 isomers)
	$C_4S-C_5S-C_6$	Benzothienothiapyran (3 isomers)
	$C_4S-C_6-C_6$	Dibenzothiophene
		Naphthothiophene (5 isomers)
		Thiophanthrene
	$C_4Se-C_6-C_6$	Dibenzoselenaphene
	$C_4Te-C_6-C_6$	Dibenzotellurophene
5,6,7	$C_4S-C_6-C_7$	Cycloheptathianaphthene
5,6,8	$C_4S-C_6-C_8$	Cyclooctathianaphthene

4-Ring Systems

5,5,6,6	$C_4O-C_4S-C_6-C_6$	Furothiophanthrene
		Benzfurothianaphthene (2 isomers)
		Furoendovinylenethianaphthene
		Thianaphthenofuran
	$C_4S-C_4S-C_6-C_6$	Thianaphthenothianaphthene (5 isomers)
		9,10-Thioanthracene
		Endovinylenebenzodithiophene
	$C_4N-C_4S-C_6-C_6$	Thianaphthenoindole (3 isomers)
		Thienocarbazole (2 isomers)
	$C_4S-C_5-C_6-C_6$	Indenothianaphthene
		Acenaphthenothiophene
5,5,6,7	$C_4O-C_4S-C_6-C_7$	Cycloheptafurothianaphthene
5,5,6,8	$C_4O-C_4S-C_6-C_8$	Cyclooctafurothianaphthene
5,6,6,6	$C_4S-C_5N-C_5N-C_6$	Thienophenanthroline
	$C_4S-C_4N_2-C_6-C_6$	Thianaphthenoquinoxaline
	$C_4S-C_5N-C_6-C_6$	Thianaphthenoquinoline
		Thienoacridine (2 isomers)
	$C_4S-C_6-C_6-C_6$	Benzothiophanthrene (5 isomers)
		Naphthothianaphthene
		Anthrathiophene (3 isomers)
		Phenanthrothiophene (5 isomers)
		Naphthisothianaphthene
		Endovinylenethianaphthene
	$C_4Se-C_5N-C_5N-C_6$	Selenophenanthroline
	$C_4Se-C_4N_2-C_6-C_6$	Selenonaphthenoquinoxaline
	$C_4Se-C_6-C_6-C_6$	Anthraselenophene
5,6,6,7	$C_4S-C_6-C_6-C_6N$	Benzothianaphthenoazepine
5,6,6,10	$C_4S-C_6-C_6-C_8OS$	(Epoxyethanothio)naphtho[1,2-*b*]thiophene
	$C_4S-C_6-C_6-C_9O$	See page 371

5-Ring Systems

5,5,5,5,14	$C_4S-C_4S-C_4S-C_4S-C_8S_4Hg_2$	See page 402
5,5,5,6,6	$C_4O-C_4S-C_4S-C_6-C_6$	Thionaphthofuran Furothianaphthenothianaphthene
	$C_4S-C_4S-C_4S-C_6-C_6$	Thienobisthianaphthene (2 isomers)
	$C_4O-C_4S-C_5-C_6-C_6$	Furoindenothianaphthene (2 isomers)
	$C_4S-C_5-C_5-C_6-C_6$	Diindenothiophene (2 isomers)
5,5,6,6,6	$C_4N-C_4S-C_5N-C_6-C_6$	Benzothianaphthenopyrrocoline Thianaphthenoquinopyrrole
	$C_4S-C_4S-C_5N-C_6-C_6$	Dithienoacridine
	$C_4S-C_4S-C_5S-C_6-C_6$	Bisthianaphthenothiapyran
	$C_4N-C_4S-C_6-C_6-C_6$	Benzothianaphthenoindole (2 isomers) Benzothienocarbazole (3 isomers)
	$C_4O-C_4S-C_6-C_6-C_6$	Furonaphthothianaphthene (2 isomers) Dibenzofurothianaphthene
	$C_4S-C_4S-C_6-C_6-C_6$	Benzobisthianaphthene (2 isomers)
	$C_4S-C_5-C_5N-C_6-C_6$	Quinolinothianaphthenocyclopentadiene
	$C_4S-C_5-C_6-C_6-C_6$	Benzindenothianaphthene (2 isomers)
5,5,6,6,8	$C_4S-C_4S-C_6-C_6-C_7O$	Dithianaphtheno[3,2-*c*]oxepine
5,6,6,6,6	$C_4S-C_5O-C_5O-C_6-C_6$	Thienobisbenzopyran
	$C_4S-C_5S-C_5S-C_6-C_6$	Thienobisbenzothiapyran (2 isomers)
	$C_4S-C_4N_2-C_6-C_6-C_6$	Naphthienoquinoxaline (2 isomers) Dibenzothienoquinoxaline
	$C_4S-C_5N-C_6-C_6-C_6$	Thianaphthenoacridine
	$C_4S-C_5O-C_6-C_6-C_6$	Spiro[isothianaphthenexanthene]
	$C_4S-C_6-C_6-C_6-C_6$	Dibenzothiophanthrene (5 isomers) Dinaphthothiophene (4 isomers) Phenanthrothianaphthene Anthrathianaphthene Pyrenothiophene

6-Ring Systems

5,5,5,5,6,6	$C_4O-C_4O-C_4S-C_4S-C_6-C_6$	Spirobi[furothianaphthene]
5,5,6,6,6,6	$C_4N-C_4S-C_5N-C_6-C_6-C_6$	Benzothianaphthenopyridindole (2 isomers)
	$C_4O-C_4S-C_6-C_6-C_6-C_6$	Benzofuronaphthothianaphthene
	$C_4S-C_4S-C_6-C_6-C_6-C_6$	Naphthothienonaphthothiophene (2 isomers)
	$C_4S-C_5-C_6-C_6-C_6-C_6$	Naphthindenothianaphthene (2 isomers) Acephenanthrylenothianaphthene

7-Ring Systems

5,6,6,6,6,6	$C_4S-C_4N_2-C_5S-C_5S-C_6-C_6$	See page 421
	$C_4S-C_4N_2-C_4N_2-C_6-C_6-C_6$	Naphthienoquinoxalopyrazine (2 isomers)
	$C_4S-C_4N_2-C_6-C_6-C_6-C_6$	Benzonaphthienoquinoxaline (2 isomers) Phenanthrothienoquinoxaline (3 isomers)
	$C_4S-C_5N-C_6-C_6-C_6-C_6$	Thianaphthenobenzacridine
5,5,5,6,6,6,6	$C_4S-C_4S-C_4S-C_6-C_6-C_6-C_6$	Benzotristhianaphthene
	$C_4O-C_4S-C_5-C_6-C_6-C_6-C_6$	Furoacephenanthrylenothianaphthene Aceanthrylenofurothianaphthene
	$C_4S-C_5-C_5-C_6-C_6-C_6-C_6$	Diacenaphthothiophene
5,5,6,6,6,6,6	$C_4S-C_5-C_4N_2-C_6-C_6-C_6-C_6$	Acenaphthonaphthienopyrazine (2 isomers)
5,6,6,6,6,6,6	$C_4S-C_4N_2-C_4N_2-C_6-C_6-C_6-C_6$	Naphthienoquinoxaloquinoxaline (2 isomers) Phenanthrothienoquinoxalopyrazine (2 isomers)

8-Ring Systems

5,5,6,6,6,6,6,6	$C_4S-C_4S-C_6-C_6-C_6-C_6-C_6-C_6$	Chrysenobisthianaphthene Pyrenobisthianaphthene (2 isomers)
5,6,6,6,6,6,6,6	$C_4S-C_4N_2-C_4N_2-C_6-C_6-C_6-C_6-C_6$	Phenanthrothienoquinoxaloquinoxaline (4 isomers)
	$C_4S-C_6-C_6-C_6-C_6-C_6-C_6-C_6$	Flavophene

9-Ring Systems

5,5,5,5,5,5,5,5,16	$C_4S-C_4S-C_4S-C_4S-C_4N-C_4N-C_4N-C_4N-C_8N_8$	See page 405
5,5,5,5,5,5,6,6,14	$C_4S-C_4S-C_4S-C_4S-C_4N-C_4N\dot{-}C_6-C_6-C_{10}S_4$	Cyclic bis-β-indolidene-bis-α-dithienyl

12-Ring Systems

5,6,6,6,6,6,6,6,6,6,6,6	$C_4S-C_5S-(C_6)_{10}$	See page 400

SUBJECT INDEX

A

1,3(2*H*)-Aceanthryleno [8,9-*f*]furo [3,4-*d*]thianaphthene, 360
Acenaphtheno [1,2-*c*]thiophene, 316
Acenaphtho [4,5-*b*]naph [1′,2′,4,5]thieno-[2,3-*e*]pyrazine, 425
Acenaphtho [4,5-*b*]naph [2′,1′,4,5]thieno-[2,3-*e*]pyrazine, 425
Acephenanthryleno [7,8-*g*]thianaphthene, 353
Anthraquinone-type dyes, 207–209
Anthra [1,2-*b*]selenophene, 457–458
—, 6,11-dimethyl, 458
6,11-Anthra [1,2-*b*]selenophenequinone, 458
Anthra [2,1,9-*cde*]thianaphthene, 351
Anthra [1,2-*b*]thiophene, 331–333
—, 6,11-dimethyl, 331
Anthra [1,2-*b*]thiophene-4,5-dicarboxylic acid, 332
6,11-Anthra [1,2-*b*]thiophenequinone, 331–333
—, 2-carboxy, 331
Anthra [2,1-*b*]thiophene, 333–334
—, 1-hydroxy, 333–334
6,11-Anthra [2,1-*b*]thiophenequinone
—, 1-hydroxy, 334
Anthra [2,3-*b*]thiophene, 331
5,10-Anthra [2,3-*b*]thiophenequinone, 331
—, 3-hydroxy, 331
6*H*-Anthra [1,9-*bc*]thiophene, 340–341
—, 1,3-dicarboxy-6-one, 340
—, 1-acetyl-6-one, 341
—, 1-carboxy-6-one, 341
Arndt-Eistert reaction, 141, 276

B

Benzidine sulfone, *see* Dibenzothiophene 5-dioxide, 3,7-diamino
12*H*-Benz [4,5]indeno [1,2-*e*]thianaphthene, 345–346
7*H*-Benz [6,7]indeno [1,2-*b*]thianaphthene, 345
Benzo [1,2-*b*, 4,5-*b*′]bisthianaphthene, 389
—, 3-chloro-6,12-dioxo-1-methyl, 389
Benzo [1,2-*b*,5,4-*b*′]bisthianaphthene, 389, 390
  derivatives of, 390
  vat dye from, 390
—, 6,12-dioxo, 390
Benzo [1,2-*b*,4,5-*b*′]dithiophene, 381, 382–383
  thioindigo dye from, 383
—, 2-methyl, 382
—, 3,7-dihydroxy, 383
Benzo [1,2-*b*,5,4-*b*′]dithiophene, 381, 383
  thioindigo dye from, 383
—, 3,5-dihydroxy, 383
Benzo [2,1-*b*,3,4-*b*′]dithiophene, 381, 383–384
  thioindigo dye from, 383
—, 3,6-dihydroxy, 383–384
Benzofuran, substitution of 3, 4–8
7,9(2*H*)-Benzo [*b*]furo [3,4-*e*]naphtho-[2,1-*g*]thianaphthene, 359
8,10(2*H*)-Benzo [*e*]furo [3,4-*b*]thianaphthene, 359
1,3(2*H*)-Benzo [*f*]furo [3,4-*d*]thianaphthene, 359
Benzo [*g*]naph [1′,2′,4,5]thieno [2,3-*b*]-quinoxaline, 424
Benzo [*g*]naph [2′,1′,4,5]thieno [2,3-*b*]-quinoxaline, 424
6*H*-Benzo [*b*]thianaphtheno [2,3-*e*]apezine, 445
12*H*-Benzo [5,6]thianaphtheno [3,2-*b*]-indole, 415, 416
7*H*-Benzo [6,7]thianaphtheno [3,2-*b*]-indole, 415, 416–417
  derivatives of, 416–417
  dipicrate of, 416
1*H*-Benzo [5,6]thianaphtheno [3,2-*b*]-pyrid [3,2,1-*hi*]indole, 419

1*H*-Benzo[6,7]thianaphtheno[3,2-*b*]pyrid[3,2,1-*hi*]indole, 419, 420
Benzo[*b*]thianaphtheno[3,2-*g*]pyrrocolline, 418
12*H*-Benzo[*g*]thieno[3,2-*a*]carbazole, 416, 417
  derivatives of, 417
12*H*-Benzo[*g*]thieno[3,4-*a*]carbazole, 416, 418
12*H*-Benzo[*i*]thieno[3,2-*a*]carbazole, 415, 417
  derivatives of, 417
12*H*-Benzo[*i*]thieno[3,4-*a*]carbazole, 416, 418
7*H*-Benzo[*e*]thieno[3,2-*b*]indole, 411, 414
—, 9-methyl, 414
10*H*-Benzo[*g*]thieno[3,2-*b*]indole, 411, 414–415
4*H*-Benzo[*b*]thieno[2,3-*d*]pyran, 361
  derivatives of, 365
5*H*-Benzo[*d*]thieno[3,2-*b*]pyran, 361, 364–365
9*H*-Benzo[*b*]thieno[2,3-*e*]thiapyran, 395
4*H*-Benzo[*b*]thieno[3,2-*e*]thiapyran, 395–396
9*H*-Benzo[*b*]thieno[3,4-*e*]thiapyran, 395, 396
  derivatives of, 396
Benzothiofuran, *see* Thianaphthene
6,11-Benzo[*b*]thiophanthraquinone, 317, 318–323
  bromination of, 320
  derivatives of, 324–325
—, 8-amino, 321
— 10-amino, 321
—, 8-bromo, 321
—, 8-chloro, 321
—, 7,8-dihydroxy, 323
—, 7,10-dihydroxy, 322, 323
—, 8,10-dihydroxy, 323
—, 9-formyl, 321–322
—, 8-methyl, 320
—, 9-methyl, 320, 322
—, 10-methyl, 320
—, 7,8,10-trihydroxy, 322
7,11-Benzo[*i*]thiophanthraquinone, 327–8
Benzo[*b*]thiophanthrene, 316–323
  derivatives of, 324–325
7*H*-Benzo[*ef*]thiophanthrene, 321
7*H*-Benzo[*ef*]thiophanthrene-7-one, 293, 341–342
Benzo[*g*]thiophanthrene, 323, 326–327
—, 7,11-dimethyl, 326
—, 11-methyl-7-iodomethyl, 326
—, 11-methyl-7-methoxymethyl, 326
Benzo[*i*]thiophanthrene, 327–328
—, 7,11-dimethyl, 327, 328
—, 9-methyl, 327
7*H*-Benzo[*jk*]thiophanthrene-7-one, 342-343
Benzo[*b*]thiophanthrone, 320
Benzo[*b*]thiophene, *see* Thianaphthene
Benzo[1,2 - *b*,3,4 - *b*′,5,6 - *b*″]tristhianaphthene, 94–95, 393
Biotin, 405, 422
Bischler-Napieralski synthesis, 429, 431
Bis-(2-dibenzothienyl) sulfoxide, 277
Bis-(3-thianaphthenacyl) sulfide, 124
Bis-(3-thianaphthenacyl) sulfone, 124
12*H*-Bisthianaphtheno[2,3-*b*,3′,2′-*e*]thiapyran, 398–399
  derivatives of, 398–399
2,2′-Bisthioindigo, 181–187
2,3′-Bisthioindigo, 187–188
3,3′-Bisthioindigo, 188–189
2,2′-Bithianaphthene, 27, 28, 54
—, 3,3′-diamino, 53–54
2,3′-Bithianaphthene, 27, 28, 54
—, 3-oxo, 94–95
2,2′-Bi-4,9-thiophanthraquinone, 293
Bromoindophenine, 206

C

Chryseno[3,2 - *b*,9,8 - *b*′]bisthianaphthene, 391–392
  vat dyes from, 391
—, 6,9,15,18-tetraoxo, 391
Claissen condensation, 144
Cyclic bis-β-indolidene-bis-α-dithienyl, 446
Cyclic 5,5,5′,5′-dimercuribis-2,2′-dithienyl, 402
1,3,6(3*H*) - Cyclohepta[*f*]furo[3,4 - *d*]thianaphthene, 359
8*H*-Cyclohepta[*g*]thianaphthene, 312
10,12(2*H*)-Cycloocta[*f*]furo[3,4-*d*]thianaphthene, 359
Cycloocta[*g*]thianaphthene, 313
3*H* - Cyclopenta[*b*]thianaphthene - 3 - one, 312
—, 1,2-dihydro 312

Cyclopenta[*b*]thiophene, 172–173
—, 4,5-dihydro-5-methyl-6-oxo, 173
Cyclohepta[*b*]thiophene-4-one
—, 4,5,6,7,8-pentahydro, 173

D

Dehydrobiotin, 405
Diacenaphtho[1,2-*b*,1′,2′-*d*]thiophene, 354
Diazine ring systems, 420–427
Diazole ring systems, 404–408
Dibenzofuran, substitution of, 10–14
5,7(2*H*)-Dibenzo[*b*,*e*]furo[3,4-*g*]thianaphthene, 359
Dibenzoselenophene, 455–457
  bromination of, 457
  derivatives of, 457
  oxidation of, 457
  physical properties of, 457
  substitution of, 10–14, 457
Dibenzotellurophene, 460–461
—, 5,5-dichloro, 460–461
Dibenzo[*fh*]thieno[3,4-*b*]quinoxaline, 423
4-Dibenzothienylacetic acid, 476
4-(2′-Dibenzothienyl)butyric acid, 274
1-(2′-Dibenzothienyl)-1,2-diphenylethylene, 237
Dibenzothienyllithium, 279
2-Dibenzothienylmagnesium bromide, 278
2.8-Dibenzothienylmagnesium bromide, 278
3-(2′-Dibenzothienyl)propionic acid, 274
Dibenzothienylsodium, 279
7*H*-Dibenzo[*b*,*ef*]thiophanthrene, 320, 321, 350–351
7*H*-Dibenzo[*b*,*ef*]thiophanthrene-7-one, 321
Dibenzo[*b*,*g*]thiophanthrene, 348
6,13-Dibenzo[*b*,*h*]thiophanthraquinone, 346
Dibenzo[*b*,*h*]thiophanthrene, 346–347
Dibenzo[*b*,*i*]thiophanthrene, 348
7*H*-Dibenzo[*b*,*jk*]thiophanthrene, 350–351
Dibenzothiophene 24, 225–282, 317, 318
  2-acyl derivatives, 269–271
  aldehyde derivatives, 268
  alkyl derivatives, 235–237
—, 2-alkyl derivatives, 236–237
  amino derivatives, 251–262
—, physical constants of, 258–259, 261–262
Dibenzothiophene (*continued*)
  analgesic action of 2-acetyl, 269
  antioxidant properties, 235
  aryl derivatives, 237
  bromination of 2- and 4-acetyl, 269
  bromo derivatives, 242–247
  carcinogenicity of 3-acetamido, 255
  chloro derivatives, 241–242, 247
  color reactions with ceric nitrate, 235
  dyes from 2-amino, 254
  dyes from 2,8-diamino, 254
  effect of HF on, 235
  history of, 227
  hydrogenation of, 232–233
  hydroxy derivatives, 262–268
    physical constants of, 266–267
  iodo derivatives, 247
  ketone derivatives, 268–272
  physical constants of, 270
  ketone derivatives, 268–272
    physical constants of 266–267
  Mannich reaction of 2-acetyl, 269
  mercuration of, 278
  metalation of, 278–282
  metal derivatives, 278–282
  nitration of 2-acetamido, 253
  nitro derivatives, 248–251
  nomenclature, 226
  occurrence in nature, 226
  organometallic derivatives, 278–282
  physical properties, 233–234
  preparation of, 227–231
  quinolinyl derivatives, 257, 260
  reduction with sodium, 232
  side chain amino derivatives, 257, 260–262
  substitution of, 10–14
  sulfones of, 237–241
  sulfoxides of, 237–238
  sulfur derivatives, 276–278
  toxicological properties, 234–235
—, 2-acetamido, 245, 252
—, 2-acetyl, 268–269, 272, 274
—, 4-acetyl, 269
—, 1-amino, 251
—, 2-amino, 247, 251, 252, 272
—, 3-amino, 245, 247, 254–255
—, 4-amino, 257
—, 2-amino-3-bromo, 252
—, 1-amino-4-methoxy, 251
—, 2-bromo, 262, 272

Dibenzothiophene (*continued*)
—, 1-bromo, 242–243
—, 2-bromo, 243–244
—, 3-bromo, 245
—, 4-bromo, 247
—, 2-(2′-carboxybenzoyl), 274, 275
—, 2-chloro, 241
—, 1-chloro-4-hydroxy, 264
—, 2-cyano, 272
—, 1,4-diacetoxy, 264, 272
—, 2,8-diacetyl, 269, 273
—, 2,8-diamino, 247, 253
—, 3,7-diamino, 255–256
—, 3,6-diamino-2,8-disulfo, 256
—, 2,8-dibromo, 244–245, 250
—, 3,7-dibromo, 244–245
—, 2,8-dibromo-dinitro, 250
—, 5-dichloride, 241
—, 2,8-dichloro, 242
—, 2,8-dihydroxy, 263–264
—, 2,8-diiodo, 247
—, 2,8-dimethyl, 236
—, 2,8-dinitro, 249
—, 2-ethoxy, 265
—, 2-ethoxy derivatives, 265, 267
—, 2-ethoxy-8-nitro, 268
—, 2-hydroxy, 262, 263, 264
—, 4-hydroxy, 264
—, 2-(1′-hydroxyethyl), 268
—, 2-iodo, 247
—, 4-iodo, 248
—, 2-methoxy, 263, 265
—, 4-methoxy, 250
—, 4-methyl, 235–236
—, 2-nitro, 243, 244, 248, 265, 277
—, 3-nitro, 249
—, 2-nitro-8-bromo, 249–250
—, 1-nitro-4-methoxy, 250
—, 3-nitro-4-methoxy, 250
—, octahydro, 232
—, 4-oxo-1,2,3,4-tetrahydro, 271
—, phenyl, 237
—, 2-propionyl, 269
—, 1,2,3,4-tetrahydro, 231, 232
—, 2-trimethylsilyl, 280–281
—, 3-trimethylsilyl, 280–281
—, 4-trimethylsilyl, 280–281
—, 4-valeryl, 271
—, 2-vinyl, 237
Dibenzothiophenecarboxylic acids, 272–276
  physical constants of, 275, 276
1-Dibenzothiophenecarboxylic acid, 272
2-Dibenzothiophenecarboxylic acid, 272
3-Dibenzothiophenecarboxylic acid, 273
—, 2-hydroxy, 263
—, 2-hydroxy, derivatives of, 273, 276
4-Dibenzothiophenecarboxylic acid, 274, 281
2,8-Dibenzothiophenedicarboxylic acid, 273
Dibenzothiophene 5-dioxide, 230, 231, 248, 274
  mercuration of, 282
  metalation of, 274, 281–282
  physical properties of, 241
  preparation of, 239
  reactions of, 239–240
—, 2-acetamido-8-ethoxy, 265
—, 2-amino, 252
—, 1-bromo, 243
—, 2-bromo, 243
—, 3-bromo, 246
—, 2-bromo-7-nitro, 250
—, 4-carboxy, 279
—, 2-chloro, 242
—, 3,7-diamino, 353, 355–356
  dyes from, 356
—, 2,8-dibromo, 244
—, 3,7-dibromo, 246, 247
—, 4,6-dicarboxy, 279
—, 2,8-dichloro, 242
—, 3,7-dichloro, 242
—, 2,8-dimethyl, 240, 241
—, 3,7-dinitro, 249
—, 3-nitro, 249
—, octahydro, 240, 241
—, 2,4,6,8-tetrahydroxy, 265
—, 2,3,7,8-tetrahydroxy, 265
—, 4-trimethylsilyl, 281
Dibenzothiophene 5-dioxide-2,8-disulfonic acid
—, 3,7-dibromo, 277
Dibenzothiophene 5-dioxide-3,7-disulfonyl chloride, 277
2,8-Dibenzothiophenedisulfonic acid, 276–277
1,4-Dibenzothiophenequinone, 264, 271–2

2-Dibenzothiophenesulfinic acid, 277
2-Dibenzothiophenesulfonic acid, 276–277
2-Dibenzothiophenethiol, 277
3,3′-Dicarboxy-2,2′-dithianaphthenyl ketone, 120
Di-(3-hydroxy-2-thianaphthenyl) ketone, 119
Diindeno[1,2-*b*,2′,1′-*d*]thiophene, 343–344
Diindeno[2,1-*b*,1′,2′-*d*]thiophene, 344
5,5,5′,5′-Dimercuribis-2,2′-dithienyl, cyclic, 402
Dinaphtho[1,2,2′,1′]thiophene, 349
Dinaphtho[2,1,1′,2′]thiophene, 349
Dinaphtho[2,1,2′,3′]thiophene, 348–349
Dinaphtho[2,3,2′,3′]thiophene, 347–348
—, 5,7,12,13-tetrahydroxy, 347
—, 5,7,12,13-tetraone, 347
Dipole moments, 16
5,6-Dithiabicyclo[2.1.1]hexane
  derivatives of, 369–370
5,7,13(3*H*)-Dithianaphtheno[3,2-*c*]oxepine, 371
Di-(3-thianaphthenyl)amine, 53, 86
3,3′-Dithianaphthenyl ketone, 117
Di-(3-thianaphthenyl)mercury, 155
Di-(3-thianaphthenyl)methane, 46
Dithieno[3,2-*a*,2′,3′-*j*]acridine, 439
Dithieno[2,3-*b*,3′,2′-*e*]-*p*-dimercurin, 401
4*H*-Dithieno[2,3-*b*,3′,2′-*e*]thiapyran, 396–398
  derivatives of, 397
  diacyl derivatives, 397–398
—, 3,5-dihydroxy-4-one, 397
  thioindigo dye from, 397
2,2′-Dithiobis-(3-nitrothianaphthene), 153–154
2,5,7,10-Dithiodimercurecin, 401–402
2,3-Dithioindoxyl, 393

E

4,8-Endovinylene[1,2-*b*,5,4-*b*′]dithiophene, 385, 389
  derivatives of, 389
—, 1,1,7,7-tetraoxide, 389
4,7-Endovinylenethianaphthene, 173
3,6-(Epoxyethanothio)naphtho[1,2-*b*]thiophene, 371

F

Fischer indole synthesis, 124, 409, 411, 415, 419
Flavophene, 354–355
Formylation of thianaphthenes, 109, 111–112
Furan, electrophilic substitution of, 2–4
Furan ring systems, 357–360
Furfural, 3
1,3(2*H*)-Furo[3,4-*d*]acephenanthryleno-[2,1-*f*]thianaphthene, 360
1,3(2*H*)-Furo[3,4-*e*]-4,8-endovinylenethianaphthene, 360
5,6,8(3*H*)-Furo[3,4-*d*]indeno[2,3-*f*]-thianaphthene, 359
5,7,11(3*H*)-Furo[3,4-*d*]indeno[3,2-*f*]thianaphthene, 359
7,9(2*H*)-Furo[3,4-*d*]naphtho[2,1-*f*]-thianaphthene, 359
6,8(2*H*)-Furo[3,4-*d*]naphtho[2,3-*f*]-thianaphthene, 359
Furo[3,4-*b*]thianaphthene, 358
1,3(2*H*)-Furo[3,4-*d*]thianaphtheno-[4,5-*f*]thianaphthene, 360
1,3(2*H*)-Furo[3,4-*b*]thiophanthrene, 358

H

Haloform reaction, 131, 132

I

Imperial Purple, 175
6*H*-Indeno[2,1-*f*]thianaphthene-4,5-dicarboxylic acid, 315–316
8*H*-Indeno[2,1-*b*]thiophene-8-one, 311
Indican, 175
Indigo, 175–176
Indigochromophore, 200
Indigoidal group, 178
Indogenide, 178
Indolignone group, 178
Indophenine, 176, 206, 210–214
  history of, 206
  leuco form, 210
  related dyes, 215–224
  structure proof, 212–213
Indophenine test, 210

Indoxyl, 175
Isatin, 175
Isoselenonaphthene, 451
—, 1,3-dioxo, 451
Isothianaphthene, 167–172
  physical constants of derivatives, 171
—, 1,3-dihydro, 167
—, 1,3-dihydro-1-methyl, 168
—, 6,7-dihydro-1,3,4-trimethyl, 168
—, 1,3-dimethyl-4-oxo-4,5,6,7-tetrahydro, 168
—, 1,3-diphenyl, 169
—, 3-ethylidene-1-oxo, 172
—, 1,3-dimethyl-4-oxo-4,5,6,7-tetrahydro, 418
—, 1-phenyl, 169
—, 1-phenyl-3-*p*-tolyl, 170
—, 1,4,6,7-tetraphenyl, 170
—, 1,3,4-trimethyl, 168–169
Isothianaphthene-1,3-dione, 172
Isothianaphthenyl sulfonium iodide
—, 1,3-dihydro-2-methyl, 167
Isothioindigo, 188–189

K

Ketone derivatives of thianaphthene, 125–130
Kolbe synthesis, 263

L

Leucothioindigos, 195–197

M

Macro nitrogen ring systems, 445–446
Macro oxygen ring systems, 371
Mannich reaction, 62, 123
Martinet rule, 200
Mercuration of thianaphthene, 154–155
Mercury ring systems, 401–402
Metalation of thiophene systems, 14–15

N

Naph[1′,2′,4,5]thieno[2,3-*b*]quinoxaline, 423
Naph[2′,1′,4,5]thieno[2,3-*b*]quinoxaline, 423
Naph[1′,2′,4,5]thieno[2,3-*b*]quinoxalo-[2,3-*e*]pyrazine, 425
Naph[2′,1′,4,5]thieno[2,3-*b*]quinoxalo-[2,3-*e*]pyrazine, 425
Naph[1′,2′,4,5]thieno[2,3-*b*]quinoxalo-[2,3-*g*]quinoxaline, 425
Naph[2′,1′,4,5]thieno[2,3-*b*]-quinoxalo-[2,3-*g*]quinoxaline, 426
5*H*-Naphth[1′,2′,2,3]indeno[4,5-*b*]-thianaphthene, 352
7*H*-Naphth[1′,2′,6,7]indeno[1,2-*b*]-thianaphthene, 352
7*H*-Naphth[1,8-*ef*]isothianaphthene-7-one, 343
Naphtho[1,8-*bc*,5,4-*b′c′*]dithiapyran, 387–388
Naphtho[2,1-*b*]thianaphthene, 160, 328–330
5,6-Naphtho[2,1-*b*]thianaphthenedicarboxylic acid, 330
Naphtho[2,1-*b′*]thieno[2,3-*d*]naphtho-[2,1-*b*]thiophene, 390–391
Naphtho[2,3-*b′*]thieno[2,3-*d*]naphtho-[2,3-*b*]thiophene, 390–391
Naphtho[1,2-*b*]thiophene, 296
  derivatives of, 297–302
  halogen derivatives, 299
  thioindigo dyes from, 302
—, 2,3-dimethyl, 297
—, 3,7-dihydroxy, 298
—, 3,8-dihydroxy, 299
—, 5-ethoxy, 299
—, 8-ethoxy, 299
—, 3-hydroxy, 298–299, 416
Naphtho[1,2-*c*]thiophene, 311
Naphtho[2,1-*b*]thiophene, 302–310
  nomenclature, 302
—, 2,2-dibromo-1-hydroxy, 306
—, 1,2-dimethyl, 303
—, 1,2-dicarboxylic acid, 303
—, 1-hydroxy, 287, 304–307
—, 1-hydroxy derivatives, 305–306, 308–309
Naphtho[2,3-*c*]thiophene, 296
—, 1,3-dimethyl-4,9-dione, 296
2*H*-Naphtho[1,8]thiophene, 310–311
2*H*-Naphtho[1,8]thiophene-3-one, 310–311
—, 8-methoxy, 311
2-Naphtho[2,1-*b*]thiophenecarboxaldehyde
—, 1-hydroxy, 306
2-Naphtho[2,1-*b*]thiophenecarboxylic acid
—, 1-phenyl, 304

—, 1-hydroxy, 306
1,3-Naphtho[2,1-*b*]thiophenedicarboxylic acid, 303
2,3-Naphtho[1,2-*b*]thiophenequinone, 299–300
  derivatives of, 301–302
1,2-Naphtho[2,1-*b*]thiophenequinone, 305, 307–308
  chloro derivatives, 308
  physical constants of, 309

O

5-Oxa-6-thiabicyclo[2.1.1]hexane
  derivatives of, 368–369
p-Oxathiene, 6
Oxindole, 175

P

Pfitzinger reaction, 436
Phenanthro[3,4-*b*]thianaphthene, 350
Phenanthro[2′,1′,4,5]thieno[2,3-*b*]quinoxaline, 424
Phenanthro[3′,4′,4,5]thieno[2,3-*b*]quinoxaline, 424
Phenanthro[9′,10′,4,5]thieno[2,3-*b*]quinoxaline, 424
Phenanthro[2′,1′,4,5]thieno[2,3-*b*]quinoxalo[2,3-*e*]pyrazine, 426
Phenanthro[2′,1′,4,5]thieno[2,3-*b*]quinoxalo[2,3-*g*]quinoxaline, 426
Phenanthro[3′,4′,4,5]thieno[2,3-*b*]quinoxalo[2,3-*e*]pyrazine, 427
Phenanthro[9′,10′,4,5]thieno[2,3-*b*]quinoxalo[2,3-*e*]pyrazine, 426
Phenanthro[3′,4′,4,5]thieno[2,3-*b*]quinoxalo[2,3-*g*]quinoxaline, 426
Phenanthro[9′,10′,4,5]thieno[2,3-*b*]quinoxalo[2,3-*g*]quinoxaline, 427
Phenanthro[2,1-*b*]thiophene, 334–335
—, 3-hydroxy, 334–335
Phenanthro[3,4-*b*]thiophene, 335–336
—, 1-hydroxy, 335–336
—, 1-hydroxy-4-isopropyl-8-methyl, 336
Phenanthro[4,3-*b*]thiophene, 336–338
  hydro derivatives, 337
—, 4,5-dicarboxylic acid, 336–337
—, 9-methoxy derivatives, 337–338
Phenanthro[9,10-*b*]thiophene, 338
—, 3-hydroxy, 338
Phenanthro[9,10-*c*]thiophene, 338–340
—, 1,3-diphenyl, 339
—, 2,3-diphenyl, 340
2,3-Phenanthro[2,1-*b*]thiophenequinone, 335
1-Phenyl-2-(3′-thianaphthenyl)ethylene, 28
2*H*-Pyrano[3,2-*b*]thianaphthene, 361
4*H*-Pyrano[3,2-*b*]thianaphthene, 361
2*H*-Pyrano[3,2-*b*]thianaphthene
  derivatives of, 362
—, 3,4-dihydro, 363
—, 2-oxo, 362
—, 2-oxo-4-carboxylic acid, 362–363
—, 2-oxo-4-methyl, 363
4*H*-Pyrano[3,2-*b*]thianaphthene, 363–364
—, 2,3-dihydro-2-oxo, 364
—, 3-bromo-2-oxo, 364
1*H*-Pyrano[3,4-*b*]thianaphthene, 361
  derivatives of, 365
Pyran ring systems, 360–367
Pyrazine ring systems, 422–427
Pyreno[4,3-*ef*,5,6-*e′f′*]bisthianaphthene, 391, 392
  vat dye from, 392
—, 7,14-dioxo, 392
Pyreno[4,3-*ef*,9,8-*e′f′*]bisthianaphthene, 391, 392
  vat dye from, 392
—, 7,14-dioxo, 392
Pyreno[2,1-*b*]thiophene, 351
Pyridazine ring systems, 420–421
Pyridine ring systems, 427–440
Pyrrole ring systems, 408–418

Q

6*H*-Quinolino[3,2-*b*]thianaphtheno-[3,2-*d*]cyclopentadiene, 437
Quinoxaline derivatives, 422–427

R

Raney nickel reduction, 32–33
Reformatsky reaction, 143
Rosenmund reaction, 109, 268
Royal Purple, 175

S

Selenoindigo dyes, 202–204, 449–450
Selenonaphthene, 447–454
  acylation of, 448
  bromination of, 448
  chlorination of, 448
  derivatives of, 452–454

Selenonaphthene (*continued*)
  nitration of, 448
  physical properties of, 452–454
  preparation of, 448
  substitution of, 8
—, 3,6-dimethyl-4,5,7-trihydroxy, 451
—, 3-hydroxy, 448, 449–450
—, nitro, 448
—, 2-(2′-pyridyl), 448
—, 2-(4′-pyridyl), 449
Selenonaphtheno[4,5-*b*]quinoxaline, 459–460
2,3-Selenonaphthoquinone, 450
4,7-Selenonaphthoquinone
—, 3,6-dimethyl, 450–451
Seleno[*lmn*][4,7]phenanthroline, 459
  derivatives of, 459
Selenophene, substitution of, 2–4
Selenopheno[2,3-*b*]selenophene, 458–459
  bromination of, 459
  picrate of, 458
Selenopheno[3,2-*b*]selenophene, 458–459
  bromination of, 459
  picrate of, 458
Selenopheno[3,4-*b*]selenophene, 458–459
  bromination of, 459
  picrate of, 458
Skraup synthesis, 430, 433
Sommelet reaction, 109
3,3′(1,1′(2*H*))-Spirobi[furo[3,4-*b*]thianaphthene-1,1-dione], 358
Spiro[isothianaphthene-1(3*H*),9′-xanthene], 366–367
Sulfide derivatives of thianaphthene, 153
Sulfone derivatives of thianaphthene, 156–166
Sulfoxide derivatives of thianaphthene, 155–156

T

Telluronaphthene, 460
—, 3-hydroxy, 460
Tetraphenylthiophene
1-Thiaindene, *see* Thianaphthene
Thianaphthene, 17–166
  acylation of, 114–124
  acyl derivatives of, 125–130
  addition complexes, 23
  alkylamino derivatives of, 58–63
  alkylation of, 17
Thianaphthene (*continued*)
  amino derivatives, 51–58
  analogs of pyrabenzamine, 59
  aryl derivatives, 26–29
  bromination of, 45–48
  carbinol derivatives, 107–108
  chlorination of, 45
  chloromethylation of, 46
  color tests for, 33
  determination of in naphthalene, 34
  dialkyl derivatives of, 24–25
  dibenzoxanthenyl derivatives of, 29
  fluorination of, 33
  halogenation of, 17
  halogen derivatives, 45–48
  hydro derivatives, 34–45
  hydrogenation of, 32–33
  iodination of, 46
  isomer formation in substitution, 8–10
  keto derivatives, 114–130
  Mannich reaction with, 17
  methyl homologs in coal tar, 19–20
  monoalkyl derivatives, 22, 24
  nitro derivatives, 48–52
  nomenclature, 18
  occurrence in nature, 18–20
  occurrence in petroleum, 20
  physical properties, 23
    of amino derivatives, 56–57, 60–61
    of aryl derivatives, 30–31
    of halogen derivatives, 47–48
    of homologs, 30–31
    of hydro derivatives, 39–44
    of hydroxy derivatives, 74–75
    of nitro derivatives, 52
  physiological activity of, 34
  polymerization of, 29, 32
  preparation of, 20–22
  removal from coal tar, 18–20
  removal from naphthalene, 33
  storage of, 29
  substitution of, 3, 4–10, 17–18
  substitution of in nitration, 9–10
  sulfide derivatives, 153
  sulfone derivatives, 156–166
  sulfoxide derivatives, 155–156
  toxicity of, 34
  trialkyl derivatives of, 25, 26
—, 3-acetamido, 84, 87
—, 3-(2-acetamidoethyl), 434

Thianaphthene (*continued*)
—, 3-acetoxy, 139
—, 2-acetyl, 116, 120, 131
  derivatives of, 125–130
  physical constants, 125–130
—, 3-acetyl, 109, 116, 132, 143
  derivatives of, 125–130
  Mannich reaction of, 123
  physical constants of, 125–130
—, 2-acetyl-5-chloro-3-hydroxy, 118
—, 2-acetyl-3-hydroxy, 118, 120, 123
—, 2-acetylcarbamyl-3-hydroxy, 119
—, 3-acetyl-2-methyl, 116
—, 2-amino, 51
—, 3-amino, 51–55, 86, 87
  preparation of, 51–53
  reactions of, 53–54
  stannic chloride salt, 52
  thioindigo dyes from, 53
—, 4-amino, 55
—, 5-amino, 55, 58
—, 5-amino-4-bromo, 55
—, 5-amino-4-phenylazo, 81
—, 2-aminomethyl, 58
—, 3-(2-benzamidoethyl), 435
—, 2-benzoyl-3-hydroxy, 118, 119
—, 2-benzoyl-3-methyl, 318
—, 2-bromo, 46
—, 3-bromo, 45, 161–162
  reactions of, 47
—, 2-bromo-3-bromomethyl, 46
—, 2-bromo-3-chloro, 155
—, 3-bromo-4,5-dihydroxy, 82
—, 2-bromo-3-hydroxy, 87
—, 4-bromo-5-hydroxy, 80–81
—, 2-bromo-3-methyl, 46
—, 2-bromo-3-nitro, 51
—, 3-bromo-2-nitro, 51
—, 3-n-butyl, 24
—, 2-carbamyl-3-hydroxy, 140
—, 5-carbethoxy-3-hydroxy-3a,4,5,6-tetrahydro, 38
—, 3-chloro, 45
—, 5-chloro, 24
—, 6-chloro, 24
—, 7-chloro, 24
—, 3-chloroacetyl, 124
—, 3-chloro-2-bromo, 46
—, 3-chloro-2-iodo, 46
—, 5-chloro-3-hydroxy, 118

Thianaphthene (*continued*)
—, 2-chloromethyl, 46, 141
—, 3-chloromethyl, 46, 108, 122, 141
—, 6-chloro-4-methyl, 45
—, 2-chloro-4,5,6,7-tetrahydro, 37
—, 3-(3′-coumarinyl), 29
—, 3-cyanatomethyl, 46
—, 3-(1-cyclohexenyl), 28
—, 3,4-diamino, 55, 58
—, 2,3-dibromo, 155
—, 3,4-dibromo-5-hydroxy
—, 2,3-dichloro, 45
—, 2,5-dichloro-6,7-dihydroxy-3-phenyl, 83
—, 2,3-dihydro, 22, 32, 33, 34–36, 160
  derivatives of, 35–36
  homologs of, 35–36
  physical properties of, 39
—, 2,3-dihydro-3-oxo-2-phenyl, 187
—, 6,7-dihydro-4-oxo-5-naphthylidenyl, 45
—, 6,7-dihydro-4-(2-thienyl), 36, 37
—, dihydroxy
  physical constants of, 85
—, 3,5-dihydroxy, 82
—, 3,6-dihydroxy, 82
—, 4,5-dihydroxy, 82
—, 4,7-dihydroxy, 83
—, 4,7-dihydroxy-5-methyl, 83
—, 6,7-dihydroxy, 83
—, 2,3-diiodo, 46
—, 2,3-dimethyl, 24
—, 2,4-dimethyl, 25
—, 3,5-dimethyl, 24, 25
—, 3-(β-dimethylaminopropionyl), 62
—, 3,4-dinitro, 49
—, 3,5-dinitro, 49, 51
—, 2,3-diphenyl, 27
—, 3-ethyl, 22, 24
—, 2-ethyl-4,5,6,7-tetrahydro, 37
—, hexachloro, 45
—, 2-hydroxy, 62–63, 135
  physical properties of, 74
  preparation of, 66
  tautomerism in, 64–65
—, 3-hydroxy, 64–66, 135, 393, 411, 412, 413, 419
  anil derivatives, 88, 93–94
  benzylidene derivatives, 88–92
  bromination of, 88, 94

Thianaphthene (*continued*)
—, 3-hydroxy (*continued*)
  condensation of in acids, 94–95
  dyes from, 86
  halogenation of, 84, 86, 88, 94
  keto form, 64–66
  physical properties of derivatives, 76–79
  preparation of, 67–73
  reactions of enol form, 84, 86–88
  reactions of keto form, 88, 93–95
  reduction of, 22
  tautomerism in, 64–66
—, 4-hydroxy, 73, 80
  reaction with Raney nickel, 80
—, 5-hydroxy, 80–82
  physical constants of, 85
—, 6-hydroxy, 81–82
  physical constants of, 85
—, 7-hydroxy, 82
—, 3-hydroxy-5-methyl, 70, 71
—, 3-hydroxy-6-methyl, 86
—, 4-hydroxy-5-methyl, 80
—, 3-hydroxy-2-nitro, 84
—, 5-hydroxy-2,3,4,6,7-pentachloro, 81
—, 6-hydroxy-3-phenyl, 81
—, 3-hydroxy-2-propionyl, 119, 120
—, 3-hydroxy-2-(2′-pyridyl), 72
—, 3-hydroxy-2-(2′-quinolinyl), 72
—, 6-hydroxy-2,5,7-tribromo, 81
—, 3-indolyl, 27
—, 2-iodo, 46
—, 3-methoxy, 120
—, 6-methoxy-2,3,5,7-tetrachloro, 81
—, 6-methoxy-2,3,7-trichloro, 81
—, 2-methyl, 22, 24, 116
—, 3-methyl, 22
—, 5-methyl, 21, 22, 24
—, 6-methyl, 24
—, 7-methyl, 24
—, 6-methyl-4-oxo-4,5,6,7-tetrahydro, 107
—, 5-methyl-3-phenyl, 26
—, 2-methyl-4,5,6,7-tetrahydro, 37
—, 3-(1′-naphthyl), 28
—, 2-nitro, 48
—, 3-nitro, 48, 50, 51
  dimer of, 48, 50, 51
  polymerization of, 32
—, 4-nitro, 49
—, 5-nitro, 49

Thianaphthene (*continued*)
—, 6-nitro, 49
—, 4-oxo-4,5,6,7-tetrahydro, 37, 45
—, 3-n-propyl, 24
—, 4-oxo-5-methyl-4,5,6,7-tetrahydro, 37
—, 4-oxo-4,5,6,7-tetrahydro, 80, 417
—, pentachloro, 45
—, 2-phenoxy-3-p-tolyl, 66
—, 2-phenoxy-3-phenyl, 27, 66
—, 2-phenyl, 26
—, 2-phenyl-4,5,6,7-tetrahydro, 37
—, 2-quinolinyl, 27
—, 3-quinolinyl, 27
—, tetrachloro, 45
—, 4,5,6,7-tetrahydro, 37–38, 45
  acylation of, 38
  physical properties of, 40–44
—, 4,5,6,7-tetrahydro-4,4,7,7-tetramethyl, 37
—, 4,5,7-trihydroxy, 84
—, 2,3,5-trimethyl, 25
—, 2,3,7-trimethyl, 25
—, 3,4,7-trinitro, 49
—, 3,5,7-trinitro, 49, 51
—, vinyl, 28
2-Thianaphtheneacetic acid, 141–142
3-Thianaphthenacetic acid, 141
7-Thianaphthenecarbonyl chloride
—, 3-hydroxy, 140–141
2-Thianaphthenecarboxaldehyde
  derivatives of, 109
—, 3-hydroxy, 87–88, 110–114
—, 3-hydroxy-6-ethoxy, 111
—, 3-hydroxy-5-methyl, 113
3-Thianaphthenecarboxaldehyde, 109, 345
  physical constants of derivatives, 115
—, 2-hydroxy, 110
3-Thianaphthenecarboxamide
—, *N*,*N*-diethyl, 132
Thianaphthenecarboxylic acids, 124, 131–153
2-Thianaphthenecarboxylic acid, 124, 131–137
  chloro derivatives of, 133–134
  derivatives of, 145–152
  physical properties of, 145–152
—, 3-amino, 137–138, 139
—, 5-amino, 103, 133, 134
—, 3-(*o*-carboxyphenyl)-5-methyl, 132
—, 3,6-dihydroxy, 141

—, 3,5-dimethyl, 132
—, 3-hydroxy, 86, 138–141
—, 5-hydroxy, 134
—, 5-hydroxy-4,6,7-trichloro, 103
—, 5-nitro, 133
3-Thianaphthenecarboxylic acid, 124, 131, 132–133, 154
  derivatives of, 145–152
  physical constants of, 145–152
—, 2-acetyl, 121
—, 2-ethyl, 133
—, 2-methyl, 133
6-Thianaphthenecarboxylic acid, 140
2-Thianaphthene-2′-coumaroneindigo, 122
Thianaphthenediacetic acid, 142
2,3-Thianaphthenedicarbonitrile, 136
2,3-Thianaphthenedicarboxamide, 136
2,3-Thianaphthenedicarboximide, 136
2,3-Thianaphthenedicarboxylic acid, 131, 134–137
  anhydride, 117
—, 5-chloro-7-methyl, 134
—, 6-ethoxy, 134
2,6-Thianaphthenedicarboxylic acid
—, 3-hydroxy, 140
4,7-Thianaphthenedicarboxylic acid
—, 4-(2′-thienyl)-4,5,6,7-tetrahydro, 38
2,3-Thianaphthenedimercuriacetate, 155
2,3-Thianaphthenedimercurichloride, 46
Thianaphthene 1-dioxide, 156
  addition reactions of, 159–163
  derivatives of, 156
  halogenation of, 160
  nitration of, 160
  physical properties of, 163–165
  polymerization of, 160
  preparation of, 156–158
  reactions of, 159–163
  reduction of, 160
  resonance of, 160
  substitution of, 10
—, 3-amino-2-carbamyl, 158
—, 3-amino-2-carbethoxy, 158
—, 2-benzoyl-3-hydroxy, 156
—, 3-bromo, 161
—, 2-bromo-2,3-dihydro, 162
—, 2-carbethoxy-3-hydroxy, 156, 158
—, 2-chloro-3-diethylamino, 162
—, 2,3-dibromo, 162
—, 2,3-dibromo-2,3-dihydro, 161
—, 2,3-dichloro, 162
—, 2,2-dichloro-3-oxo, 162
—, 2,3-dihydro, 160–163
—, 3a,7a-dihydro, 163
—, 2,3-dihydro-6-nitro, 161
—, 3-hydroxy, 156, 157, 158
—, 3-methoxy, 157, 158
—, 6-nitro, 49
Thianaphthene-α-glucuronic acid, 143
3-Thianaphtheneglyoxal, 109–110
2-Thianaphtheneglyoxalic acid
—, 3-hydroxy, 118
2-Thianaphthene-2-indoleindigo, 110
3-Thianaphthene-2-indoleindigo, 110
Thianaphthene-4-one
—, 2-phenyl-4,5,6,7-tetrahydro, 26
Thianaphthene 1-oxide
—, 2-bromo-3-chloro-, 155
—, 2,3-dibromo, 155, 156
—, 2,3-dichloro-2,3-dihydro, 155
2-Thianaphthenemercurichloride
—, 3-chloro, 46
Thianaphthenequinones, 95–107
2,3-Thianaphthenequinone, 95–102, 122, 404
  2-anils of, 88, 93–94
  derivatives of, 98–99
  phenylhydrazones of, 97
  physical constants of, 98–99
  reaction with Raney nickel, 101
  thioindigo from, 96–97
  thioindirubin from, 96–97
—, 6-chloro-4-methyl, 121
4,5-Thianaphthenequinone, 102–104
  physical constants of, 106
—, 3-bromo, 82, 104
—, 2-carboxy-6,7-dichloro, 103
—, 7-sulfo, 102
—, 2,3,6,7-tetrachloro, 103
4,7-Thianaphthenequinone, 84
4,7-Thianaphthenequinone, 104–107
  physical constants of derivatives, 106
—, 7-anil-3-bromo-5-hydroxy, 104
—, 5-hydroxy, 84, 105
—, 5-hydroxy-6-methyl, 107
—, 5-methoxy, 105
—, 5-methyl, 105, 107
—, 6-methyl, 107
6,7-Thianaphthenequinone, 104
—, 2,5-dichloro-3-phenyl, 104, 106

Thianaphthenesulfonic acids, 153
3-Thianaphthenesulfonic acid, 153
Thianaphthenium picrate, 70
Thianaphtheno[3,2-*c*]acridine, 438
Thianaphtheno[5,6-*b*]benzofuran
—, 3-hydroxy, 358
Thianaphtheno[2′,3′,4,5]benz[1,2-*c*]acridine, 438–439
Thianaphtheno[2,3-*b*][1,3]dioxole, 101, 367
Thianaphtheno[6,7-*b*][1,3]dioxole
  derivatives of, 367–368
10*H*-Thianaphtheno[3,2-*b*]indole, 411–413
  derivatives of, 412–413
—, 5-dioxide, 411–412
Thianaphthenol, *see* Thianaphthene, hydroxy
4*H*-Thianaphtheno[3,2-*d*]-*m*-oxazine, 443, 444–445
4*H*-Thianaphtheno[2,3-*e*]-*m*-oxazine, 443–444
2-Thianaphthenone
—, 2,3-dihydro-3,3-diphenyl, 100
—, 2,3-dihydro-3,3-di-*p*-tolyl, 100
3-Thianaphthenone
  2-benzylidene derivatives of, 88–92
—, 2,3-dihydro-2,2-diphenyl, 100
Thianaphthenones
  diaryl derivatives of, 100
2,3-Thianaphthenoporphyrazine, 136
1*H*-Thianaphtheno[3,2-*c*]pyrazole, 406–407
  derivatives of, 406–407
  sulfones from, 406–407
  reduction of sulfones of, 407
Thianaphtheno[2,3-*d*]pyridazine, 420
Thianaphtheno[3,2-*b*]pyrazine
—, 2,3-dicyano, 423
Thianaphtheno[2,3-*c*]pyridine, 432, 434–435
Thianaphtheno[3,2-*d*]pyrimidine, 421–422
2*H*-Thianaphtheno[2,3-*c*]pyrrole, 408, 410
Thianaphtheno[3,2-*b*]quinoline, 435–436
1*H*-Thianaphtheno[2,3-*d*]quino[1,8-*ab*] pyrrole, 418, 419
Thianaphtheno[2,3-*b*]quinoxaline, 423
1*H*-Thianaphtheno[5,4-*b*]-*p*-thiazine, 442–443
4*H*-Thianaphtheno[5,6-*b*]-*p*-thiazine, 442, 443
Thianaphtheno[3,2-*b*]thianaphthene, 385–386
Thianaphtheno[4,5-*f*]thianaphthene, 385, 386
  thioindigo dye from, 386
—, 5-chloro-3,6-dihydroxy, 386
Thianaphtheno[5,4-*d*]thianaphthene, 385, 386–387
  thioindigo dye from, 386
  trinitrobenzene complex, 387
—, 1,6-dihydroxy, 386
Thianaphtheno[5,4-*f*]thianaphthene, 385, 387
Thianaphtheno[7,6-*f*]thianaphthene, 385, 387–388
  thioindigo dye from, 387
—, 3,8-dihydroxy, 387
Thianaphtheno[2,3-*d*]thiazole, 440
Thianaphtheno[3,2-*d*]thiazole, 440, 441
Thianaphtheno[4,5-*d*]thiazole, 440, 441
Thianaphtheno[7,6-*d*]thiazole, 440, 441–442
2*H*-Thianaphtheno[2,3]triazole, 404
—, 2-phenyl, 404
2-(2′-Thianaphthenoyl)benzoic acid, 319
2-(3′-Thianaphthenoyl)benzoic acid, 319
3-Thianaphthenylacetonitrile, 108, 144
3-Thianaphthenylalanine, 58–59
1 - (3′ - Thianaphthenyl) - 3 - amino - 3-methylbutane, 62
1 - (3′ - Thianaphthenyl) - 2 - amino - 2-methylpropane, 62
4-(3′-Thianaphthenyl)butyramide
—, 2,2-dimethyl, 143
4-(3′-Thianaphthenyl)butyric acid, 142
2-Thianaphthenylcarbinol, 46, 107
3-Thianaphthenylcarbinol, 107–108, 133
  benzoate ester, 107
—, 2-methyl, 108
3-Thianaphthenylcinchoninic acids, 31, 123
3-(3′-Thianaphthenyl)crotonic acid
  ethyl ester, 143
  methyl ester, 143
3-Thianaphthenyldiphenylacetic acid, 108, 142

3-Thianaphthenyldiphenylcarbinol, 108
—, 2-bromo, 108
2-(3′-Thianaphthenyl)ethanol, 59, 108
2-(3′-Thianaphthenyl)ethylamine, 59
2-(3-Thianaphthenyl)ethyl bromide, 46, 123
3-Thianaphthenylglycolic acid
—, phenyl, 153
3-Thianaphthenylglyoxal, 123
3-Thianaphthenylglyoxalic acid, 153
  esters of, 144
2-Thianaphthenyllithium, 109
4-(3-Thianaphthenyl)-2-mercaptothiazole, 124
3-Thianaphthenylmercuriacetate, 154–155
Thianaphthenylmethylimidazoline, 62
3-Thianaphthenyloxyglucoside, 86
2-(2′-Thianaphthenyl)-1-phenyl-1-cyanoethylene, 109
3-(3′-Thianaphthenyl)propionic acid, 142
3-(2′-Thianaphthenyl)propionic acid
—, 3′-hydroxy, 144
3-Thianaphthenylpyruvic acid, 153
  derivatives of, 144
Thianaphthenyl sulfides, 153
2,2′-Thianaphthoin
Thianthrene, 231
Thiapyran ring systems, 394–401
Thiaquindoline, 435–436
Thiazine ring systems, 442–443
Thiazole ring systems, 440–442
Thieno[2,3-*c*]acridine, 435, 436–437
Thieno[3,2-*c*,4,5-*c*′]bis[1]benzopyran, 365–366
12,13(2*H*)-Thieno[3,2-*b*,4,5-*b*′]bis[1]benzothiapyran, 399, 400
  derivatives of, 400
11,13(2*H*)-Thieno[3,2-*b*,4,5-*b*′]bis[1]benzothiapyran, 399
—, 11,13-dioxo, 399
Thieno[2,3-*b*,3,2-*d*]bisthianaphthene, 393
Thieno[3,2-*b*,2,3-*d*]bisthianaphthene, 393
12,13(2*H*)-Thieno[2,3-*b*,5,4-*b*′]bis[1]thiapyran-12,13-dione, 421
10*H*-Thieno[3,2-*a*]carbazole, 411, 413–414
  complex salts, 414
  derivatives, 413–414
10*H*-Thieno[3,4-*a*]carbazole, 411, 415
  derivatives of, 415
Thieno[3,4-*c*]cinnoline, 420, 421
Thieno[2,3-*c*]furan, 358
1,3(2*H*)-Thieno[3,4-*c*]furan, 358
1*H*-Thieno[3,4-*b*]imidazole, 404, 405
  derivatives of, 405
2*H*-Thieno[2,3-*f*]indazole, 405–406
2*H*-Thieno[3,2-*g*]indazole, 406, 407–408
  derivatives of, 407–408
  thioindigo dye from, 407–408
4*H*-Thieno[3,2-*b*]indole, 408–410
  derivatives of, 409–410
Thieno[3,4-*c*][1,2,5]oxadithiole, 370
Thieno[2,3-*d*]oxazole, 443
Thieno[3,4]-*p*-dioxin
  derivatives of, 368
2,3-Thienoporphyrazine, 445–446
Thieno[*lmn*][4,7]phenanthroline, 439–440
2*H*-Thieno[2,3-*b*]pyran, 360–361
—, 4,6-dimethyl-2-one, 360–361
5*H*-Thieno[3,2-*b*]pyran, 361
  derivatives of, 361
3*H*-Thieno[3,4-c]pyrazole, 404
Thieno[2,3-*b*]pyridine, 427, 430–431
  bromination of, 431
  thioindigo dye from, 431
—, 4,6-dimethyl, 430
—, 3-hydroxy, 431
—, 5-nitro, 431
Thieno[3,2-*b*]pyridine, 427, 428–429
  derivatives of, 428–429
  thiopyrindigo from, 428
Thieno[2,3-*c*]pyridine, 427, 431–432
Thieno[3,2-*b*]pyridine
—, 3-hydroxy, 66
Thieno[3,2-*c*]pyridine, 427, 429–430
Thieno[3,4-*c*]pyridine, 427, 432, 435, 437
Thienopyridineindigos, 204
5*H*-Thieno[2,3-*c*]pyrrole, 408
Thieno[2,3-*c*]quinoline, 432, 433
Thieno[2,3-*f*]quinoline, 432, 434
Thieno[2,3-*g*]quinoline, 432, 433
Thieno[3,2-*b*]quinoline, 432, 433
Thieno[3,2-*f*]quinoline, 432, 434
Thieno[3,2-*b*]thianaphthene, 381–382
4*H*-Thieno[2,3-*b*]thiapyran, 394
  derivatives of, 394
7*H*-Thieno[2,3-*c*]thiapyran, 394–395
  derivatives of, 395
Thienothioindigo, 378

Thieno[2,3-*b*]thiophene, 372–381
  acylation of, 375
  carboxylic acid derivative, 376
  chemical properties, 374–377
  dipole moment of, 374
  nitration of, 376
  physical constants of derivatives, 380
  preparation of, 372–373
  quinoline derivative, 377
  substitution of, 10
Thieno[3,2-*b*]thiophene, 372–381
  acylation of, 375
  carboxylic acid derivative, 376
  chemical properties, 374–377
  dipole moment of, 374
  nitration of, 376
  physical properties of, 378–379, 381
  physical properties of derivatives, 380
  preparation of, 373
  substitution of, 10
Thieno[3,4-*b*]thiophene, 372, 373, 378
—, 3-hydroxy-4,6-dimethyl, 378
Thienothiophenes, substitution of, 10
9,10-Thioanthracene, 385, 388
—, 9,10-dihydro-9-phenyl, 388
Thioindican, 86
Thioindigo, 93, 175–224
  commercial dyes from, 182–185
  determination of, 199
  Friedländer's synthesis of, 181
  leuco form, 195–197
  nomenclature, 178–180
  preparation of, 181–194
  sulfones of, 156
  symmetrical dyes, 181, 186–189
  trans configuration, 180
  vatting of, 195–197
—, 6-chloro-6′-ethoxy-4-methyl, 96
—, 6,6′-dichloro, 96
—, 5,5′-dimethyl, 71–72
Thioindigo dyes, 175–224
  bibliography for, 215–224
  factors affecting color, 199–206
  halogenation of, 199
  nitration of, 198
  oxidation of, 197–198
  patent bibliography, 216–224
  preparation of asymmetrical, 189–194
Thioindigo dyes (*continued*)
  production of, 177
  reactions of, 197–199
  sulfonation of, 198
Thioindigo white
—, 2,2′-dimethyl, 187
—, 2,2′-diphenyl, 187
Thioindigo whites, 179, 195–197
Thioindirubin, 93, 187–189
  nomenclature, 178–180
Thioindogenides, 194
Thioindoxyl, *see* Thianaphthene, 3-hydroxy
1,4-Thionaphthalene, 381, 384–385
  derivatives of, 384–385
Thionaphthen, *see* Thianaphthene
4,9-Thionaphtho[2,3-*c*]furan, 360
2,3-Thiophanthraquinone, 286, 287, 288
  derivatives of, 294
4,9-Thiophanthraquinone, 285, 286, 288–295
  derivatives of, 295
  physical constants of, 295
  preparation of, 289
—, 5-amino, 293
—, 6-amino, 290
—, 5-amino-2-chloro, 292
—, 2-bromo, 292
—, 2-carboxy, 292
—, 5-carboxy, 293
—, 2-chloro, 289
—, 5-chloro, 291
—, 2-methyl, 289
—, 3-methyl, 289
Thiophanthrene, 284
  alkyl derivatives of, 284–285
  aryl derivatives of, 285–286
  derivatives of, 294
  nomenclature, 284
  physical constants of, 294
—, 9-carboxy-3-hydroxy, 287
—, 2,2-dibromo-3-hydroxy, 287
—, 2,7-dimethyl, 285
—, 4,9-dimethyl, 285
—, 9-ethoxy-3-hydroxy, 287
—, 3-hydroxy, 286–288, 416
—, 3-hydroxy-9-methyl, 287
—, 2-naphthyl, 285
2,3-Thiophanthrenedicarboxylic acid, 286

Thiophene, electrophilic substitution of, 2–4
$\alpha,\beta,\alpha',\beta'$-Thiophenobis(thiochromone)-azine, 421
Thiophthenes (see 3 isomeric thienothiophenes), 372–381
Triazole ring systems, 404
Trifluoromethylethylene, 7
Tyrian Purple, 175

V

Vitamin K, 102, 107

W
2519